VOL. XXXV. NO. 3. JANUARY, 1942.

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Proceedings of the Royal Society of Medicine

Chairman—A. M. H. GRAY, C.B.E., M.D., President of the Society

OCCASIONAL LECTURE

[*Delivered on December* 12, 1941]

On the Need for Abandoning Much in Immunology that has been Regarded as Assured

By Sir ALMROTH E. WRIGHT, M.D., F.R.S.

PART I

TECHNIQUE

IT will be well to deal first with the methods which have been employed in these researches.

(1) *An Improved Technique for Making a Glass Pricker*

Three forms of glass prickers can be used for drawing blood from the finger.

The *first* is the ordinary glass pricker which is made by drawing out a piece of glass capillary tube, without giving the matter any special attention, in the peep flame of a Bunsen burner. The conical pricker so obtained has every possible demerit. It opens up a minimum of capillaries, and so furnishes very little blood; and it takes toll for what little blood it gives in the form of a good deal of pain—for the rapidly expanding cone, which follows upon the sharp point, forcibly prises the tissues asunder.

The *second* form of glass pricker is the *gouge pricker,* which was suggested by the late Dr. Clemenger, one of my fellow-workers. This is made by inserting a pin into the open end of a capillary tube, and breaking away its walls, first on one side and then on another, until the capillary tube, which was originally cylindrical, has been converted into a sharp-pointed gouge.

The *third* form is the *sliver pricker* which is illustrated in figs. 1 and 2. This consists of a pointed, thin, lancet-shaped blade which goes in almost painlessly and gives, because it cuts across a great number of capillary vessels a copious flow of blood. The method of making a *sliver pricker* is shown in fig. 2.

We begin by choosing a fairly stout capillary pipette, and preferably one which runs out, as shown in the figure, into an eccentrically disposed stem. We then take a *sharp*

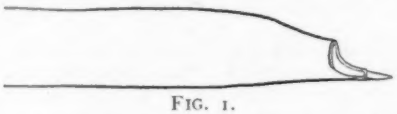


FIG. 1.

glass-cutting knife or a writing diamond and make a *very short* and *very superficial* scratch on the upper surface of the neck of the pipette before it runs out into the stem. This done, we, holding the pipette in the position shown in the diagram, place our thumb-nail underneath the lower wall of the capillary stem about 2 cm. from the scratch and then bring upward pressure to bear here, while downward pressure is, so as to make this point the fulcrum, applied to the upper wall of the capillary stem at a point about 2 cm. distally to where the thumb-nail is placed.

By this procedure we split off a sharply pointed and very thin sliver from the lower wall of the capillary tube. With a pricker of that kind it is quite easy to obtain 1 c.c. or even more of blood from one or more almost painless pricks made at the base of the finger-nail.

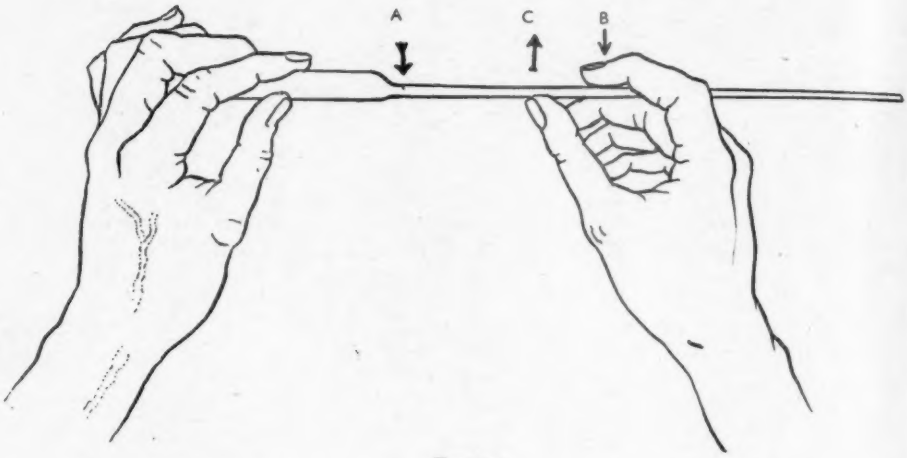


FIG. 2.

A = Superficial cut. B = Point at which downward force is applied. C = Point at which upward force is to be applied.

(2). *On an Improved Technique for Washing Blood Corpuscles on a Centrifuge, and for Obtaining in as Short a Time as Twenty Seconds a Corpuscular Sediment Containing a very Large Percentage of Leucocytes*

The method of washing blood corpuscles prescribed in my "Technique of the Teat and the Capillary Glass Tube" consisted in collecting blood direct from the finger into about six or eight times its volume of salt solution; and then centrifuging twice over until in each case all the corpuscles have been brought down. This technique can be improved upon.

One of the demerits of the method just described is that centrifugalization of the unclotted blood will, if it is not arrested betimes, bring down blood platelets into the first, and again into the second corpuscular deposit.

The presence of platelets in a phagocytic mixture must be avoided for platelets reduce, and may—as was shown ten or more years ago by my then fellow-worker Dr. E. J. Storer—entirely abolish phagocytosis.

A corpuscular deposit free from platelets can always be obtained by preparing our washed corpuscles from defibrinated blood instead of from blood taken direct from the finger.

A second blemish on the method is that it involves two centrifugalizations; and complete centrifugalizations occupy a considerable time.

This can be avoided if we, before proceeding to wash our corpuscles, defibrinate our blood and then centrifuge and pipette off the serum.

The corpuscular sediment is then transferred to a centrifuge tube about 10-12 cm. long which holds sufficient salt solution to dilute the corpuscular deposit 25 or more times. Under these conditions a single washing will reduce the serum in the corpuscular deposit to a perfectly negligible amount.

It is important to note that it is unnecessary to continue the centrifugalization for more than twenty to twenty-five seconds. By that time very large numbers of leucocytes will have been carried to the bottom and the corpuscular deposit will be far richer in leucocytes than was the blood with which we started.

The more rapid carrying down of the leucocytes in the centrifugalized salt solution is no doubt due to their somewhat smaller specific gravity being more than offset by their larger dimensions and spherical shape.

(3) *On the Employment of Centrifugalization for Bringing the Microbes and Leucocytes in a Phagocytic Mixture into More Effective Contact than when these are Allowed to Gravitate Down Together in Capillary Tubes Laid on Their Side in an Incubator*

Centrifugalization provides, as becomes obvious the moment the idea suggests itself, a much better agency for bringing the microbes into contact with the leucocytes than did the original technique of laying the capillary pipettes on their side in an incubator and letting the leucocytes settle down, through the microbes suspended in serum.

The advantages of centrifugalization over sedimentation are:

(1) Centrifugalization undertaken at the laboratory temperature and continued for only a minute or even less than a minute gives always a larger phagocytic intake than gravitation conducted at blood heat and prolonged for the usual quarter of an hour.

(2) Again, when we centrifuge phagocytic mixtures containing microbes, normal washed corpuscles and normal salt solution, we obtain always a small amount of spontaneous phagocytosis; while gravitation in the incubator gives an almost completely blank result. This holds true unless the incubation is unduly prolonged when another factor, to which attention will be drawn later, comes into consideration.

(3) Again, when we are dealing with a phagocytic mixture composed of microbes, washed leucocytes and heated serum centrifugalization gives us a bacterial ingest of fully one-third of that given by the original (unheated) serum, whereas gravitation in the incubator gives, when heated serum is employed, an almost negligible phagocytic intake.

(4) Finally, when we are dealing with blood which has given only a small epiphylactic response to an *in vitro* inoculation, gravitation in the incubator not infrequently gives a blank result, whereas centrifugalization gives one which is definitely positive.

The following points in connexion with centrifugalization of phagocytic mixtures require to be kept in mind:

(1) Centrifugalization can be carried out effectively at ordinary room temperature.

(2) The phagocytic mixture should (it must, of course, be enclosed in a capillary tube which is sealed off at either end) be centrifuged first for about forty-five seconds in one direction and then for the same time in the reverse direction. But the centrifuge may be arrested as soon as ever we have a sharp line of demarcation between the corpuscular sediment and the supernatant fluid of the phagocytic mixture.

(4) *On the Elimination of all Unphagocytosed Microbes from the Phagocytic Mixtures by Amputating, after Centrifugalization, the Upper Ends of the Capillary Tubes*

The capillary tubes which contain the phagocytic mixtures are, after centrifugalization, amputated at the line of demarcation between the sediment and the supernatant fluid.

But we have now in our amputated tubes a solid and intractable mass of corpuscles; and we must, if we want to make good films, bring our corpuscles into suspension in an equal volume of a not too viscid fluid: Having diluted a small portion of the serum which was pipetted off from our centrifuged defibrinated blood with an equal volume of normal salt solution; and having provided ourselves with an "evacuating pipette" (an evacuating pipette is a simple capillary pipette drawn out into a stem of sufficient fineness to go to the bottom of our amputated tubes) we inscribe upon its stem a fiducial mark at a point which will provide about sufficient room for housing the amount of corpuscular sediment provided in a single tube. We then aspirate from each amputated capillary tube in turn all the corpuscular sediment and then take up into our pipette an equal volume of diluted serum. We then blow these quanta out on to a paraffined slide, and, after mixing, proceed to make our films. In drawing off the corpuscular sediment from our amputated capillary tubes care must be taken to stop off the inflow into our pipette immediately the supply of corpuscles is exhausted, for a sudden indraft of air would scatter the corpuscular deposit all over the interior surface of the pipette.

(5) *On the Omission from the Phagocytic Count of the Uncountably Large Numbers of Microbes which may be Ingested by Individual Leucocytes when the Microbes in the Phagocytic Mixture are Agglutinated by the Serum Employed*

Attention has not, up to the present, been directed to the fact that staphylococci may be

agglutinated when either a heated serum, a reconstituted serum,[1] or a heated leucocytic diffusate[2] is employed in a phagocytic mixture in lieu of an ordinary unheated serum.

The agglutination becomes more marked when Tuberculin B.E. is brought into application upon the microbes along with a heated serum.

These facts touching agglutination would appear to have, in addition to their bearing on phagocytic testing, a general importance; for they obviously suggest that the leucocytes are one, and for all we know the only, source of the agglutinins which appear in the blood of those who are making epiphylactic response to vaccines, or, as the case may be, auto-inoculations.

Agglutination of microbes shows itself in a phagocytic film in the unduly small percentage of the leucocytes which have ingested microbes, and in the fact that there are often among the leucocytes which have phagocyted many which have gorged themselves with more microbes than it is possible to count. The blank leucocytes are, of course, those whose environment has been swept clean of microbes by the agglutinating action of the serum; and the phagocytes whose protoplasm is completely full of microbes are, of course, those which have chanced upon a mass of agglutinated microbes.

And when we have this condition of things—in other words, when we have only an unduly small percentage of phagocytosing leucocytes with a considerable proportion of leucocytes brim-full of microbes—it is good practice to discard the whole count as one vitiated by bacterial agglutination.

But if we hesitate to condemn an entire film on the ground of a few leucocytes which have gluttonized, we should either leave out of our count these particular leucocytes, or else we should by way of a compromise (and I have in this paper adopted this compromise) accredit them with having ingested each 20, or some arbitrarily chosen, large number of microbes.

Table I gives the results of differential phagocytic counts of films made from phagocytic mixtures containing my unheated non-agglutinating, and my heated and agglutinating, and my reconstituted and agglutinating serum; and the corresponding sera of a colleague.

TABLE I.—DETAILS OF THE STAPHYLOCOCCIC INTAKE OF A.E.W.'S AND K.B.R.'S LEUCOCYTES IN PHAGOCYTIC MIXTURES MADE RESPECTIVELY WITH THEIR UNHEATED, HEATED AND RECONSTITUTED SERUM.

	A.E.W.'s leucocytes			K.B.R's leucocytes		
	Percentage of polynuclears which have ingested a countable number of microbes	Percentage of polynuclears which have ingested an uncountable number of microbes	Percentage of blank cells	Percentage of polynuclears which have ingested a countable number of microbes	Percentage of polynuclears which have ingested an uncountable number of microbes	Percentage of blank cells
Experiment 1						
Unheated serum	94	6	0	96	0	4
Heated serum	78	2	20	78	4	18
Reconstituted serum[1]	60	11	29	76	18	6
Experiment 2						
Unheated serum	97	3	0	84	0	16
Heated serum	53	11	36	36	0	64
Reconstituted serum	37	14	49	57	24	19

NOTE.—I have elsewhere reported (*Lancet*, 1931 (ii), 277, Table XIX without being able to account for it, the almost incredibly large phagocytic ingests which are obtained in phagocytic mixtures composed of washed corpuscles, staphylococcus suspensions and a heated serum to which effective quanta of Tuberculin B.E. have been added. I cited for instance (loc. cit. Table XIX) an experiment in which with different

[1] By a *reconstituted serum* I mean a solution of euglobulin obtained by precipitating normal human serum with 10 volumes of water saturated with CO_2, collecting the precipitate by centrifugalization and re-dissolving it in a volume of normal salt solution which corresponds to the volume of the original serum.

[2] A *leucocytic diffusate* is an extract of leucocytes such as is obtained by digesting washed corpuscles at blood temperature in normal salt solution.

quanta of Tuberculin B.E. 8 to 48% of the polynuclear leucocytes were completely filled with microbes.

In later experiments I have seen with similar phagocytic mixtures nearly 100% of the polynuclear leucocytes absolutely gorged with staphylococci.

Results of this sort which previously were unaccountable find now an easy explanation in the fact that both Tuberculin B.E. and heated serum agglutinate the staphylococci of phagocytic mixtures, while both operate also as phagocytic "stimulins".

(6) *On a Procedure which Admits of a Rough Discrimination of the Role Played in "Phagocytic Mixtures" by (a) the Opsonic Action Exerted by the Serum on the Microbes; (b) a Phago-incitor Stimulin Action Exerted by the Serum upon the Leucocytes; and (c) the Phago-incitor Action Exerted upon the Leucocytes by the Microbes which were previously Credited with being an Inert Phagocytic Pabulum*

The traditional procedure for measuring phagocytic power does not distinguish between those three chemical activities. It does not even contemplate the possibility of any except an opsonic chemical action taking place in phagocytic mixtures.

Much can be learned on this question by carrying out the phagocytic tests in two operations instead of in one.

In the original phagocytic procedure equal parts of washed normal corpuscles, of the patient's serum, and of the microbic suspension were taken, and note was taken of the compendial result achieved.

In the procedure which I propose to subsitute for purposes of exploring the triple action just referred to (I propose to call it the *Cæsuric* Procedure) we—*this constitutes our first operation*—mix equal volumes of (*a*) serum and microbic suspension, or (*b*) serum and washed corpuscles, or (*c*) microbic suspension and washed corpuscles. Let us call these pre-phagocytic mixtures.

We then, after incubating the above pre-phagocytic mixtures for fifteen minutes, pass to our *second operation*. If we are dealing with a "*sero-opsonic*" *pre-phagocytic mixture*, we add to 2 volumes of it, 1 volume of washed corpuscles. If we are dealing with a "*sero-stimulin*" *pre-phagocytic mixture* we add to 2 volumes of it, 1 volume of microbes. And if we are dealing with a *microbi-leucocytic pre-phagocytic mixture* we add to 2 volumes of it 1 volume of serum. We then reincubate for fifteen minutes, thus bringing those chemical agents which have been operating in our pre-phagocytic mixtures a *second time* into action in completed phagocytic mixtures.

Tables V and IX show that the cæsuric procedure furnishes valuable information.

Obviously the method would be more valuable if the adventitious chemical action which comes into operation in the secondary incubation could be eliminated.

There are two methods by which this might be done:

The *first* would be to centrifuge the phagocytic mixture, as soon as the third of the triad of operative factors have been added. By thus avoiding second incubation we should cut out most, if not all, the adventitious chemical action.

The *second* device—which could be combined with the first—would be to employ when testing a serum for stimulins, a bacterial pabulum of pre-opsonized microbes.

My experience is that we gain little, if indeed anything, by these devices; and for two reasons, *first* because allowing as we do in the first case, less time for opsonization and stimulin action, we greatly reduce our phagocytic count.

And, if our second device gives us no better results, it is because we, by furnishing the leucocytes with a bacterial pabulum of pre-opsonized microbes, obtain an all-round increase in phagocytosis.

And that, like the all-round decrease of phagocytosis obtained by the first device, largely obliterates phagocytic differences.

Part II

The Evidence against the Present Universally Accepted Doctrines of Phagocytosis and Immunization

Introductory

Douglas and I showed in our original paper on the opsonic power of the serum that the phagocytosis which occurred when washed corpuscles, microbes and serum were brought together was due to the serum acting upon the microbes in such a way as to prepare them for ingestion.

After establishing the fact that the blood fluids converted the microbes into an attractive pabulum for the leucocytes (whence the word "opsonin"), and further showing that this property is abolished, or all but abolished, by heating the serum to 60° C., we went on to test by what we called the "chiastic procedure" the serum and washed corpuscles of two patients, whom we had successfully treated with staphylococcus vaccine, against the serum and corpuscles of normal men.[1]

In the chiastic procedure here in question four separate phagocytic mixtures are made all containing a volume of one and the same staphylococcus suspension. To the volume of staphylococcus suspension employed in capillary *Tube 1* are added equal volumes of *Normal Serum*, and of *Normal Washed Corpuscles;* to that employed in *Tube 2*, equal volumes of *Normal Serum* and of the *Patient's Washed Corpuscles;* to that in *Tube 3*, equal volumes of the *Patient's Serum* and of *Normal Washed Corpuscles;* and to the staphylococcus suspension employed in *Tube 4*, equal volumes of the *Patient's Serum* and of his *Washed Corpuscles.*

It emerged in experiments done in this way on the bloods of our two patients that there was no improvement in their corpuscles but a distinct improvement in their sera. And we drew from these and from similar experiments in which the serum and corpuscles of tubercular patients were compared with those of normal men, the conclusion that epiphylactic responses such as those which are induced by therapeutic inoculations that do not cause constitutional disturbances, and by the auto-inoculations of apyrexic patients, increase the opsonic power of the serum, and leave the leucocytes unchanged.

It ought, of course, to have suggested itself to us that what we had found in patients examined ten days after inoculation might not hold true of such patients examined earlier; and further that what we had found to hold true of apyrexic patients would not necessarily hold true of those suffering from pyrexic infections.

Also it ought to have suggested itself to us *as possible* that the blood of our inoculated or auto-inoculating patients might, or at any rate might in certain cases, contain in addition to bacteriotropic substances (opsonins) leucocytotropic substances which would, acting as stimulins or depressants, raise or lower the efficiency of the phagocytes.

Again, it never even occurred to us that the epiphylactic response of the blood which follows upon the inoculation of vaccines and upon auto-inoculations, could affect any but the particular variety of microbe which was evoking the response.

And finally, it never dawned upon us that the microbes which were employed to serve as a bacterial pabulum and to furnish a measure of phagocytic power, could play any active part in the phagocytic reaction.

All these a priori inferences were mistaken, and we were, as has only recently emerged, just as much out of our depth with regard to what was happening in our phagocytic mixtures, as to what was happening in our patients.

I do not make light of these errors. "Errors", Goethe tells us, "always matter; but how very much they matter becomes clear to a man only at the end of his way." But I realize that if I were put back into the blinkers which confined my outlook and that of my contemporaries forty years ago, I—I do not want to shelter myself by saying we—should almost certainly fall again into the same pitfalls.

It had, at that time, been recently demonstrated by Ehrlich that epiphylactic response was *antithetic chemical response.* And it seemed to follow from this that inoculations of bacterial vaccines (and I would add the engendering of auto-inoculations) would produce only bacteriotropic as distinguished from leucocytotropic substances. And again it seemed to follow by analogy from the fact that the antitoxins produced by toxins are strictly specific that the same would hold also of bacterial inoculations.

Again, forty years ago, it had not occurred to anyone that epiphylactic response could be evoked *in vitro.* And much less had it suggested itself that epiphylactic response *in vitro* would come under regular observation in all phagocytic, and (as is evidenced in the 'Caput and Cauda phenomenon')[2] in all hæmo-bactericidal tests.

And to-day I often ask myself how much water will flow under the bridges before that fundamental fact that epiphylactic response occurs in the blood *in vitro* succeeds in getting itself into bacteriological textbooks.

Let me now proceed to deal in detail with some of the more important points which have been incidentally referred to.

[1] *Proc. Roy. Soc.*, 1903, **72**; *ibid.*, 1904, **73**.

[2] *vide* Wright, New Principles in Therapeutic Inoculation, *Lancet*, Feb. 24, 1923, and also *infra* p. 178[4].

THERMOLABILITY OF OPSONINS

Only about a year after Douglas and I had shown that opsonins of normal serum are largely thermolabile, Neufeld and Rimpau[1] announced that the heated serum of "immune animals" contained phago-incitor substances, which rendered the pneumococci and streptococci with which he had inoculated his animals, phagocytable or, as the case may be, more phagocytable.

There were in the ratiocinative operations of these authors two main false assumptions.

The *first* was the assumption that animals which have been heavily and repeatedly inoculated may without further question be called "*immune*"; and that their sera may properly be described as "*immune*"; or "anti-sera".

I pointed out thirty-five years ago[2] that these so-called "immune sera" might in lieu of, or along with, epiphylactic substances produced in the organism, contain antigenic substances remaining over in the blood from the original inoculations or auto-inoculations.

I have nothing to alter in that except that where I, thirty-five years ago, wrote antigens I should now probably write "leucocytic stimulins". And whichever of these descriptive terms I applied to such bacterial substances as might still be circulating in the blood, it would be clear that these would, when transferred to another animal organism, confer on it instead of passive, *active* immunization.

A conspicuous, but now forgotten, practical exemplification of active immunization misinterpreted as a passive one was furnished by the beneficial results which Chantemesse (this was twenty-five or thirty years ago) claimed in typhoid fever from the inoculation of an "antityphoid serum". Of this so-called anti-serum he administered in heavily infected cases of typhoid fever reduced, and in still more heavily infected cases absolutely minimal doses—doses of not more than a fraction of a cubic centimetre. (I was unable to procure from him a sample of the serum he was using in order to see whether it contained antigens or antibodies.)

These considerations apply just as much to the sera of Neufeld and Rimpau's laboratory animals as to the sera of horses employed for the treatment of human patients.

A *second fallacious assumption* made by Neufeld and Rimpau was that convincing proof of a phago-incitor serum operating as an opsonin is furnished when a serum ceases, after it has been digested with heavy doses of the antigenic microbes, to exert its previous phago-incitor effect.

It has to be kept in view in connexion with all such *absorption experiments* that when a serum is digested with a bacterial culture, and the microbes are afterwards removed by centrifugalization, there may remain in the serum such a charge of bacterial toxins as would, even with opsonins present, paralyse phagocytosis.

In view of that consideration "absorption tests" can never furnish convincing proof that a serum contained, before it was operated upon, opsonic substances.

A year after the publication of Neufeld and Rimpau's work Reid and I,[3] following up the work of these observers, found phago-incitor substances in the heated serum of auto-inoculating tubercular patients. These "phago-incitor substances" I—avoiding the term "bacteriotropins"[4] which Neufeld and Rimpau had applied to them—called "thermostable opsonins".

We were, in calling the phago-incitor substances we were dealing with "thermostable opsonins", beguiled by the self-same fallacies which had misled Neufeld and Rimpau.

[1] Neufeld and Rimpau, *Deutsche med. Wchnschr.*, Sept. 1904.

[2] A Criticism of the Foundations of Serum Therapy, *Clin. Journal*, May 16, 1906. (Reprinted in the Author's "Studies in Immunisation", Constable, 1909.)

[3] Wright and Reid, *Proc. Roy. Soc. B.*, 1906, **77** (Also reprinted in the Author's "Studies in Immunisation", Constable, 1909.)

[4] I eschewed the term "bacteriotropins" because I had already five years before (*Lancet*, Dec. 23, 1899, 1st paragraph) employed that term in its proper generic signification, i.e. as a name for *every and any substance which enters into chemical combination with microbes*. And the use to which Neufeld and Rimpau put this term is also, quite apart from the question of priority of usage, a perfectly improper use. This will be seen when we regard the fact that the limitation of the term *bacteriotropins* to one special variety of "bacterio-tropic" substances is as wrong in principle as would be the limitation of a zoological class—let us say the class "*Mammalian*" to one particular species of mammals.

In other words we had no better warranty for concluding that the heated sera of our anto-inoculating tuberculous patients contained opsonins, than the fact that they induced phagocytosis; and the further fact that the phagocytic power of these sera was lost, when they were digested with heavy doses of tubercle bacilli.

But when I look back on the fact that many of our tuberculous patients were in a very unwholesome condition I cannot help thinking that their blood may not infrequently have contained instead of, or along with, opsonins, tuberculin derived from the tubercle bacilli in their system. And such tuberculin would, as will be shown presently, operate as a phagocytic stimulin.

Further points—and these are new points—which invalidate Neufeld and Rimpau's argument that they had in hand a thermo-stable opsonic serum are referred to below.

I have in view the point that a serum may (as is shown in Table V) be converted into a leucocyte-stimulating serum by heating; and also the point that heating may (as has been shown in Table I) convert sera which do not agglutinate staphylococci into sera which do, with the result that both the percentage of phagocytes and the number of microbes phagocyted may be greatly increased—this being explained by the fact that leucocytes are not attracted by chemotaxis to individual staphylococci to anything like the same degree as they are to agglomerated staphylococci.

The next important happening in the field of phagocytic research was that Shattock and Dudgeon[1]—employing the same chiastic method that Douglas and I had done, but conducting their experiments with a "phagocytic pabulum" consisting of melanin particles—found that the leucocytes of patients suffering from febrile infections differ from those of normal men in that they have usually a *supra-* —but occasionally an *infra-normal* phagocytic efficiency.

And Shattock and Dudgeon pointed out that no one could, in view of their having worked with a phagocytic pabulum of melanin particles, come to any other conclusion than that the increased leucocytic response obtained by auto-inoculations was non-specific.

We shall return to this question of non-specific response to bacterial infections later. In the meantime let us note that the results obtained by Shattock and Dudgeon are irreconcilable with Erhlich's theory that immunizing response consists *exclusively* in the production of antithetic chemical substances.

For a long time after the date of Shattock and Dudgeon's publication—an interval during which I was working in succession on the study of therapeutic inoculation applied to tuberculosis, prophylactic inoculation against pneumonia, and the treatment of war wounds—I was turning over in my mind not only Shattock and Dudgeon's findings, but also the many new facts about epiphylactic response which my work was bringing to light. And the conviction was steadily growing in my mind that much of the currently accepted doctrine of immunization was erroneous.

Finally, after much tentative work, I obtained convincing proof of non-specific (i.e. *homo-* and *hetero-*) bactericidal response to the implantation of vaccines into the blood *in vitro*.

It was shown in the papers cited below[2] that separate implantations of staphylococcus and streptococcus vaccines into the blood *in vitro* resulted in a notable increase in the bactericidal power exerted by serum upon both these microbes.

And let me here remind the reader, though the recent advances in chemotherapy may have deprived this of much of its interest, that in both those papers I drew attention to the fact that the power of inducing epiphylactic response in extravascular blood had put into our hands a method of transfusion—I called it *immuno-transfusion* from which good results were to be expected in the treatment of septicæmia.

Also I pointed out in this connexion that the blood which was used for immuno-transfusion might be either normal blood subjected to vaccine treatment *in vitro;* or, if this was preferred, blood obtained from a donor who had been inoculated a few hours before

[1] Shattock and Dudgeon, *Proc. Roy. Soc. B.*, 1908, **80**.

[2] Wright, Sur la production de substances bactericides non-specifiques au moyen des vaccine *in vivo* et *in vitro*. *Compt. rend. Acad. d. sc.*, t. **167**, 600, Oct. 21, 1918. Wright, A Lecture on the Lessons of the War, delivered at the Royal Society of Medicine on Feb. 25, 1919, *Lancet*, March 29, 1919.

with a staphylococcus or streptococcus vaccine[1]—the optimum dosage of the vaccine used having in each case been ascertained by what I call "a vaccine response test".

About the same time I obtained clear evidence of leucocytes killing microbes extracellularly.

EXPERIMENTAL EVIDENCE SHOWING THAT LEUCOCYTES KILL MICROBES EXTRACELLULARLY

The procedure by which it was first established that leucocytes can kill extracellularly was described and figured in my paper "On the Lessons of the War" referred to above.

The procedure consists in taking leucocytes which have emigrated on to glass laths from blood centrifuged before it clots and disposing these laths—one directly as it comes out of the serum, and the other after the serum has been washed off—upon an agar plate inseminated with staphylococcus or streptococcus. When the implanted plates are then incubated the staphylococcus grows out all over the surface of the agar, except under these central strips of each lath where we have a thick belt of emigrated leucocytes. There the agar surface, both in the case where the leucocytes are operating in serum and in the case where they are operating in salt solution, remains absolutely bare.

When the laths are now stained and microscopically examined, it is found that in the case where the leucocytes were operating in serum every leucocyte is full of staphylococci, and these have (we may assume) been inhibited in their growth or killed intracellularly.

On the other hand, in the specimen where the leucocytes were operating in salt solution the leucocytes are empty of microbes, and here the staphylococci have manifestly been inhibited in their growth or killed extracellularly.

I have confirmed the fact that the leucocytes exert their bactericidal power extra- as well as intra-cellularly by five other experimental methods.

I shall label them Procedures 2, 3, 4, 5, and 6.

Procedure 2.—Staphylococci in moderate numbers are implanted into blood drawn off from the finger. (Moderate numbers would in this case mean some thousands or tens of thousands of staphylococci per cubic centimetre.) This blood is immediately centrifuged in flat "emigration tubes"[2] and is thus divided into an upper portion consisting of plasma, which is presently converted into a *white clot*, and a lower portion consisting of red blood corpuscles surmounted by a cap of leucocytes—this portion being presently converted into a *red clot*. The centrifuged blood is now, after the emigration tube has been very tenderly capped with plasticine, placed upright in a plasticine slide in the incubator; and incubation is continued for twenty-four hours.

When the clot is now microscopically examined, it is found that many of the implanted staphylococci (but not by any means all of them, for a large proportion are killed instantaneously in the blood) have grown out into colonies in the white clot.

But it is the distribution of the colonies, as distinct from the bactericidal power of the blood, which is of special interest. The colonies are found to have grown out in considerable numbers in the distal portion of the white clot; but that none (this will of course depend upon our having hit off the proper measure of *in vitro* infection) will have grown out in the leucocyte invaded proximal area of the white clot or—this is the relevant point—in the area which lies immediately distal to that into which the leucocytes have penetrated. In that "no man's land" there are, as microscopic examination shows, neither leucocytes nor microbes. The microbes which should by rights have grown out there must have been killed by bactericidal substances excreted by the leucocytes.

Procedure 3.—Here we make "extra-" and "intra-coagular implantations" of staphylococcus into blood in capillary tubes. An *intra-coagular implantation is* made by inoculating staphylococcus into blood drawn from the finger, aspirating this inoculated blood into capillary tubes and allowing it to clot undisturbed.

[1] Immuno-transfusion in this latter form has, as I gather from the French medical literature of the twenty-two years 1918-1940, given very striking results. In England the method has as good as never come into application. And I myself have had only one good opportunity of administering to a patient blood inoculated *in vitro*. This was at the end of the last war, when I was dealing with a severe case of septicæmia following a wound infection. An account of the very strikingly beneficial result achieved in that case was included in the second of the two papers referred to above.

[2] The method of making these is described in the "Technique of the Teat and Capillary Pipette", Wright and Colebrook, Constable, London, 1921.

In an *extra-coagular implantation* a similar volume of *unimplanted* blood is drawn up into a capillary tube, and we then, after the clot has contracted and the serum has exuded, implant into this serum the same volume of staphylococcus suspension as was employed for the intra-coagular implantation—let us say 5 c.mm. of a 10,000-fold dilution of a twenty-four-hour broth culture. We make the implantation with the aid of a capillary pipette drawn out into a hair-fine extremity.

Along with the two foregoing implantations a similar quantum of staphylococcus suspension is implanted into another capillary tube which contains only serum. These tubes—let me for convenience number them 1, 2, and 3—are, after sealing up, incubated horizontally (horizontally to prevent the colonies running together) upon a plasticine slide.

After twenty-four hours' incubation the staphylococcic colonies in Tube 3, which contains only serum, are seen to be many times more numerous than those in the extra-coagular serum in Tube 2. These are so few that they can quite easily be counted by the naked eye.

Dealing now with Tube 1, the colonies which have grown out in the interior of the clot are enumerated as follows: The clot is blown out into a test tube of water. This is then placed in a water bath standing at 60° C., and the clot is left there until it is fully decolorized. After that it is transferred to a slide; is fixed down upon this by drying, and is then lightly stained with methylene blue. This done the colonies are counted under the low power of the microscope.

These, instead of being, as one might have expected, definitely fewer than those in the ex-coagular serum, are generally a little more numerous.

With regard to the interpretation of the findings, those in Tube 2 point to stimulins deriving from the microbes implanted into the serum operating upon the leucocytes of the clot, and causing these to pour out bactericidal elements. These will now diffuse into the serum, rendering this bactericidal. And the fact that the colonies which grow out in the clot are, despite the presumptively better opportunity for phagocytosis there afforded, fewer than those which have grown out in the serum in Tube 2, is no doubt due to the bactericidal substances which have been excreted by the leucocytes coming less effectively into operation upon the microbes which are lodged in the clot than on the microbes which are floating free in the serum.

Procedure 4.—We draw up some melted agar into the stem of a capillary tube and then immediately blow it out. We leave by this procedure a coating of agar upon the wall of our capillary tube. We then draw up into this a volume of blood from the finger and set this aside to clot and contract. By this contraction the agar lining is pulled off from the walls of the tube and the serum now exudes through the agar capsule into the extra-coagular space. Into this space we introduce by the same procedure which was employed for extra-coagular implantations, a small measured quantum of staphylococcus suspension.

At the same time we—to provide ourselves with a control—make a similar implantation of staphylococci into two samples of serum and draw these up the one into a naked and the other into an agar-lined tube.

After twenty-four hours' incubation we find that the colonies which have grown out in the control tubes containing only serum are much more numerous than those which have grown in the serum in the tube containing the agar-enveloped clot. And we must, as in Procedure 3, assume that the leucocytes of the clot have (under the impulsion of bacterial stimulins which have traversed the agar capsule) secreted bactericidal substances which have killed the microbes which are implanted into the serum outside.

Procedure 5.—Here we prepare one or more *leucocyte-lined capillary tubes.* This is done by drawing up into our capillary tube first a very small quantum of normal salt solution and then about sufficient blood to occupy about one-half of the stem, and after this another very small quantum of normal salt solution. The purpose of flanking the blood above and below with salt solution is to prevent the clot drying and fixing itself on to the walls of the tube.

After filling in our pipette as explained we seal up its distal end, mark off with a blue pencil the limits of our blood-clot, and then incubate. After some twenty to thirty minutes we blow out the clot and run enough normal salt solution through the tube to carry away loose leucocytes and red blood corpuscles. We then aspirate into our tube some serum lightly implanted with staphylococcus, disposing this so that the serum

shall fill up the space between our two blue pencil marks, and extend on each side a little distance beyond them. We then take exactly the same amount of our staphylococcus implanted serum and draw this up into an unlined capillary tube. This done we seal up the distal ends of our pipettes in the flame, and provide against evaporation from the proximal ends by blocking the neck of our capillary pipette either with a little mercury, or with a little salt solution. We then place our pipettes in the incubator, fixing them down horizontally upon a plasticine slide.

Comparison of the tubes twenty-four hours after shows that a great number of staphylococci have been killed in the leucocyte-lined tube, and it will be noticed that the bactericidal effect exerted by the leucocytes extends some little distance on each side beyond the blue pencil marks.

The experiment can be repeated with even more striking results with capillary tubes which have been furnished with a double lining of leucocytes—such a double lining being obtained by refilling the tube after Clot No. 1 has been blown out with a new lot of blood and then carrying out the rest of the technique exactly as in the single leucocyte-lined tube.

Procedure 6.—We here first prepare some defibrinated blood and then add to 100 c.mm. of this blood one-tenth of its volume of approximately a 30,000-fold dilution of a twenty-four-hour broth culture of staphylococcus. 10 c.mm. of such a 30,000-fold dilution will represent an implantation of about 100 staphylococci per cubic centimetre of blood.

We now take three to six capillary tubes; draw up into each 100 c.mm. of the implanted blood; amputate the barrels of the pipettes; and then centrifuge until the corpuscles have been carried down completely. That done, and there will now be just as many microbes in the upper as in the lower layers of the serum, we block the proximal ends of the tubes with plasticine and then incubate them upright in plasticine slides for one and a half to two hours.

We now take a series of evacuating pipettes (one for each tube) and draw out the distal end of each stem into a throttle—taking care to make this sufficiently wide. This done we mark off in each tube the middle point of the contained serum with a blue pencil, and then, working very cautiously, draw up into our evacuating pipette, first the upper, and then, after interposing an air-bubble, the lower half of the serum.

This done, we seal up the stems of our evacuating pipettes above and below, and arrange them horizontally upon a plasticine slide; and now incubate for twenty-four hours. After that we count the colonies which have developed in each portion of the serum (Table II).

TABLE II.

	Number of staphylococcus colonies which developed in centrifuged serum taken from the distal half of the tube	the proximal half of the tube
Defibrinated blood heavily implanted with staphylococci	Uncountable	60
Defibrinated blood implanted with half as many staphylococci	100 100	0 11
Defibrinated blood implanted with roughly a quarter as many staphylococci	41 23	8 10

The point that leucocytes can be killed quite as surely extracellularly as intracellularly settled, let me now take up the question as to whether the doctrine of Shattock and Dudgeon that the leucocytes of pyrexic, i.e. auto-inoculating patients have generally acquired a leucocytic efficiency superior to that of the leucocytes of the normal blood, should prevail over the doctrine which was enumerated by Douglas and myself. I mean the doctrine that the leucocytes are unaffected by inoculation.

QUESTION AS TO WHETHER THE LEUCOCYTES ARE OR ARE NOT AFFECTED BY INOCULATION

With a view to clearing up this point I, employing as before, the chiastic procedure, compared *my own defibrinated blood untreated* with *my defibrinated blood inoculated in vitro* with doses of $\frac{1}{1000000}$ to $\frac{1}{500000}$ of its volume of a Tuberculin B.E.[1]

The inoculated and the control bloods were then incubated side by side for longer or

[1] The Tuberculin B.E. which was employed here and in all the other experiments reported in this paper contained 1 mg. of dried and ground up tubercle bacilli per cubic centimetre of fluid.

shorter periods. After that they were centrifuged; the serum pipetted off, and the corpuscles washed in normal salt solution. Chiastic phagocytic mixtures were then made of the washed corpuscles and the sera in the manner particularized in the table below.

TABLE III.—SHOWING THE EFFECT OF CHIASTIC EXPERIMENTS IN WHICH THE WASHED LEUCOCYTES AND SERUM OF NORMAL DEFIBRINATED BLOOD WERE COMPARED WITH THE WASHED LEUCOCYTES AND SERUM OF THE SAME DEFIBRINATED BLOOD TREATED WITH TUBERCULIN B.E.

The test-microbes employed were staphylococci, and the interpretation of the Initials employed is given at the foot of the table.

Amount of Tuberculin B.E.	Period for which the inoculated and control bloods were incubated	Constitution of the phagocytic mixtures	Phago-cytic count	Summary of results
$\frac{1}{1000000}$ of a suspension containing 1 mg. of dried tubercle powder in 1 c.c.	25 minutes	NS + NC + Staph.	3·29	Phagocytic efficiency of my blood increased as 1 : 2·4; that of my leucocytes as 1 : 2 ; and the phago-incitor power of my serum as 1 : 1·2
		NS + IC + Staph.	6·70	
		IS + NC + Staph.	3·96	
		IS + IC + Staph.	8·01	
Ditto	20 minutes	NS + NC + Staph.	1·09	Phagocytic efficiency of my blood increased as 1 : 2; that of my leucocytes as 1 : 2 ; the phago-incitor power of my serum remaining as 1 : 1
		NS + IC + Staph.	2·16	
		IS + NC + Staph.	1·04	
		IS + IC + Staph.	2·06	
Ditto	Not noted (Probably between 20 and 40 minutes)	NS + NC + Staph.	3·24	Phagocytic efficiency of my blood increased as 1 : 1·7; that of my leucocytes as 1 : 1·4 ; the phago-incitor power of my serum remaining as 1 : 1, nearly
		NS + IC + Staph.	6·72	
		IS + NC + Staph.	5·20	
		IS + IC + Staph.	5·60	
Ditto	Not noted (Probably between 20 and 40 minutes)	NS + NC + Staph.	1·34	Phagocytic efficiency of my blood increased as 1 : 2·1; and that of my leucocytes as 1 : 1·2 ; and the phago-incitor power of my serum increased as 1 : 1·7
		NS + IC + Staph.	1·70	
		IS + NC + Staph.	2·38	
		IS + IC + Staph.	2·80	
Ditto	40 minutes	NS + NC + Staph.	7·1	Phogocytic efficiency of my blood increased as 1 : 1·1, and that of my leucocytes as 1 : 1·3 ; and the phago-incitor power of my serum reduced as 1 : 0·9, nearly
		NS + IC + Staph.	9·7	
		IS + NC + Stayh.	6·4	
		IS + IC + Staph.	8·1	
$\frac{1}{5000000}$ mg.	40 minutes	NS + NC + Staph.	3·9	Phagocytic efficiency of my blood increased as 1 : 1·5; that of my leucocytes remains as 1 : 1, nearly ; and the phago-incitor power of my serum is increased as 1 : 1·4
		NS + IC + Staph.	5·1	
		IS + NC + Staph.	6·4	
		IS + IC + Staph.	6·0	

NS = Normal Serum ; NC = Normal Corpuscles ; IS = Immune Serum ; IC = Immune Corpuscles.

Epitome of Results.—Phagocytic efficiency of the whole blood improved on the average as *1 : 1·7;* ***Phagocytic efficiency of the leucocytes*** improved on the average as *1 : 1·5;* ***Phago-incitor power of the serum*** improved on the average as *1 : 1·2;* and in two of the experiments as 1 : 1·7 and 1 : 1·4 respectively.

These results show that Douglas and I were wrong in concluding that the leucocytes are not affected by bacterial vaccines, and that Shattock and Dudgeon were, on the whole, right in concluding that they were.

Further, the results set forth in the above table show—and this is in agreement with

the inferences of Shattock and Dudgeon—that the increase of phagocytic efficiency which is obtained by bacterial vaccines is non-specific.

More direct confirmation of Shattock and Dudgeon's inferences has been obtained by my sometime pupil—Dr. Ronald Hare of Toronto—by the phagocytic testing of the leucocytes with different kinds and strains of microbes. These unpublished results, which have been very generously placed at my disposal, are set out in the table below.

TABLE IV.—SHOWING THE NON-SPECIFIC RESPONSE OF LEUCOCYTES TO SEPTICÆMIC INFECTIONS.

Here the Washed Corpuscles of Infected Patients and of Normal Controls were incubated with 1 volume of normal serum and 1 volume of a suspension of 2, 3, or 4 different strains or species of microbes.

The results of the phagocytic counts so made are shown in the table below in the form of ratios—the phagocytic intake of the normal man being in each case represented by 1.

Name of patient	Streptococcus Strain 1	Streptococcus Strain 2	Streptococcus Strain 3	Staphylococcus
Boon (mild streptococcus infection)	1·8	1·8		1·7
Ellis (fatal streptococcal septicæmia)	0·73	0·76		0·8
Same patient (a week later) ...	0·2	0·3	0·17	0·1
Hatcher (Whitlow)	0·49	0·51		0·47
Barker (streptococcal infection) ...	1·3			0·8
Allan (acute fatal streptococcus septicæmia)	1·9	2·5		2·3

THE EFFECT EXERTED BY HEATING THE SERUM FOR TEN MINUTES TO 60° C.

The problem of the nature of the thermostable phago-incitor substances found by Neufeld and Rimpau in the heated serum of their "immune animals" and by Reid and myself in the heated sera of tuberculous patients, calling for further investigation, my choice of methods lay between testing the heated sera by the "Absorptional" and by the "Cæsuric Method". And inasmuch as the former method is, as has been indicated above, very fallacious when employed as a prelude to phagocytic tests, I naturally employed the latter.

I took a series of samples of my serum and tested these unheated and heated, both by the "sero-microbic", and by the "sero-corpuscular cæsuric procedure". Table V shows the results yielded by these two different methods.

TABLE V.—SECTION 1 SETS OUT THE RESULTS OF PHAGOCYTIC TESTS OBTAINED BY MAKING, TO BEGIN WITH, "SERO-MICROBIC, PRE-PHAGOCYTIC", AND SECTION 2, THE RESULTS BY MAKING, TO BEGIN WITH, "SERO-CORPUSCULAR, PRE-PHAGOCYTIC MIXTURES"; AND THEN AFTERWARDS COMPLETING THESE MIXTURES.

	Phagocytic counts obtained in consecutive experiments Serial No. of the Serum Test: 1	2	3	4	5	6	7	8	9	Average
SECTION 1										
Sero-microbic Cæsuric method										
Here the UNHEATED SERUM was incubated first for 15′ with a suspension of staphylococci; and then, after leucocytes had been added, the completed phagocytic mixtures were incubated for another 15′	1·75	3·9	6·0	3·5	6·6	1·83	2·1	1·7	6·7	3·8
Here the same procedure was repeated with HEATED SERUM	0·12	1·15	1·6	1·5	0·85	0·42	0·38	1·3	3·2	1·3
SECTION 2.										
Sero-corpuscular Cæsuric method										
Here the UNHEATED SERUM was incubated first for 15′ with a suspension of washed corpuscles; and then after staphylococci had been added the completed phagocytic mixtures were incubated for another 15′	1·61	1·38	4·7	1·8	0·64	3·0	1·2	0·21	2·0	1·83
Here the same procedure was repeated with HEATED SERUM	1·85	3·4	7·3	2·0	2·9	5·0	1·95	1·9	2·85	3·1

In the first section of Table V it will be seen that the opsonic power of the serum is, as was previously found by Douglas and myself, very much reduced by heating. The figures set forth in the second section of the table throw, however, fresh light upon the question, for they show that heating does a great deal besides reducing the opsonic index of the serum. It, as the figures show, converts the serum into a powerful leucocytic stimulin. It is therefore probable that *some* (one does not know how much) of the phago-incitor action, which was attributed by Neufeld and Rimpau to a "*bacteriotropin*" and by Reid and myself to "*thermostable opsonins*" may have been attributable to "*thermo-generated stimulins*".

I leave that question for a moment to consider another fundamental point which I and my fellow-workers elicited with regard to phagocytosis in our original researches on that subject—researches which we may, using an apt expression of Francis Bacon, call our *Vindematio Prima* or "*First Grape-harvesting*".

We had concluded in that Vindematio Prima that leucocytes did not ingest microbes in the absence of serum; in other words that leucocytes could not be credited with the faculty of spontaneously phagocyting microbes.

That question obviously required to be re-examined. For our original findings might quite well hold of normal leucocytes, and yet not hold of the leucocytes of auto-inoculating patients. And that, as the results displayed in Table VI (Columns 2 and 3), and VII, and VIII show, is what we do actually find.

TABLE VI.—SPONTANEOUS PHAGOCYTOSIS TO STAPHYLOCOCCI—COMPARISON OF NORMAL LEUCOCYTES WITH THOSE OF AUTO-INOCULATING PATIENTS.

Technique.—The washed corpuscles derived from defibrinated bloods are mixed in each case with an equal volume of an 8 to 12-fold dilution of a twenty-four-hour broth culture of staphylococcus. These mixtures are then centrifuged for forty-five seconds in one direction and then for forty-five seconds in the opposite direction. The supernatant fluid is then amputated and film preparations made from the corpuscular deposit.

About 200 leucocytes are then counted in each specimen and the average staphylococcic intake of the individual leucocytes is determined in the ordinary way by dividing the total number of microbes ingested by the number of leucocytes counted.

Single observations of normal men		Single observations of febrile and non-febrile patients suffering from:			
A. S.	0·04	Gonorrhœa	0·86	Strept. septicæmia	0·25
D. S.	0·03	Gonococcal arthritis	0·88	Puerperal fever—Case 1	0·25
C. W. M.	0·01	Rheumatism—Case 1	0·25	Puerperal fever—Case 2	0·22
F. H.	0·02	Rheumatism—Case 2	0·48	Puerperal fever—Case 3	0·15
A. E. W.	0·02	Rheumatism—Case 3	0·11	Puerperal cellulitis	0·20
A. H.	0·02	Chancre	0·60	Septic pneumonia	0·19
E. A. B.	0·05	Secondary syphilis	0·22	Febrile cellulitis	0·20
K. B. R.	0·05	Endocarditis—Case 1	0·26	Mastoid infection	0·55
		Endocarditis—Case 2	0·70	Appendicitis with peritonitis	0·27
		Endocarditis—Case 3	0·70	Cervical abscess	1·00
		Tubercular peritonitis	0·35	Hæmorrhagic colitis	0·16
Average	0·03	Average	0·4 (nearly)		

TABLE VII.—SPONTANEOUS PHAGOCYTOSIS IN (FOR THE MOST PART FEBRILE) PHTHISIS.

The technique here used was the same as that employed above.

Average result of the observations made with the leucocytes of normal men	Results of single observations made upon febrile and non-febrile phthisical patients			
0·03	Case 1	1·59	Case 10	0·20
	,, 2	0·54	,, 11	0·37
	,, 3	0·21	,, 12	0·37
	,, 4	0·54	,, 13	0·10
	,, 5	1·80	,, 14	0·54
	,, 6	0·50	,, 15	1·50
	,, 7	0·13	,, 16	0·74
	,, 8	0·10	,, 17	1·20
	,, 9	0·06	,, 18	0·86
Average 0·03			Average 0·65	

In view of these data it is obvious that we should, if we had not already been compelled to do so by Shattock and Dudgeon's work and by the data set out in Table III, have had

to delete from our immunological code the pronouncement that leucocytes are unaffected by inoculation.

And it emerges from comparative observations which now run into hundreds that we get on the whole much better information about immunizing response by testing the leucocytes of an infected patient than by testing his serum. Also we get our results with much less trouble.

An example of epiphylactic response to an inoculation of Tuberculin B.E. is furnished in the table below.

TABLE VIII.—SPONTANEOUS PHAGOCYTOSIS OF STAPHYLOCOCCUS BY THE WASHED CORPUSCLES OF A PATIENT IN THE LAST STAGES OF PHTHISIS; BEFORE AND AFTER THE INOCULATION OF TUBERCULIN B.E.

25.10.32	Before inoculation	1·58
	Inoculation of $\frac{\text{B.E.}}{3{,}000}$	
25.10.32	Two hours after inoculation	0·63
27.10.32		3·26
31.10.32		2·03
9.12.32	Six hours before death	0·32

The point of superiority which this method has over all others is that incubation is avoided, and with that, almost all the possibility of auto-inoculation *in vitro*.

Another point of very practical interest which emerges from consideration of the data set forth in the tables above is that we have here an unfallacious method of determining what dose of vaccine to administer to a patient to evoke the best epiphylactic response.

STIMULINS

The term "*stimulins*" was introduced by Metchnikoff; and what he had in view when he spoke of a "stimulin" was a product of active immunization which circulated in the blood of immune animals and men and which operated by "training" the leucocytes to attack the species of microbes which had supplied the immunizing ictus. In other words a "stimulin" as conceived by Metchnikoff was a kind of hormone engendered in the animal body in response to an inoculation or auto-inoculation.

It will be appreciated that thermo-generated stimulins of serum which have been considered above belong to a category of stimulins which have nothing in common with those which Metchnikoff had in mind, except only the fact that they are leucocytotropic and not bacteriotropic—that is to say they operate on the leucocytes instead of combining chemically with the microbes. But they differ from Metchnikoff's notion of a stimulin is not being generated in response to an immunizing ictus. And this holds true even more emphatically of the bacterial antigens which come under consideration in the next table.

That bacteria and bacterial derivatives function as leucocytic stimulins may be said to be a priori probable, and experimental confirmation of this deduction is as a matter of fact very easily obtained.

One of the simplest ways of doing this is to make cæsuric phagocytic experiments such as those set out in Table IX. Here there was made (A) an ordinary compendial phagocytic mixture; and (B) a phagocytic mixture made by adding 1 volume of serum to 2 volumes of a microbi-corpuscular pre-phagocytic mixture which had been incubated for fifteen minutes.

TABLE IX.

	Phagocytic counts obtained in experiments No.					
	1	2	3	4	5	Average
A. Here the microbes, leucocytes and serum were incubated, all of them together for 15 minutes	3·9	1·4	0·63	0·44	1·4	1·55
B. Here the microbes and leucocytes were incubated first for 15 minutes by themselves; and this microbi-corpuscular pre-phagocytic mixture was, after it had been by the addition of serum, converted into a phagocytic mixture, reincubated for another 15 minutes	6·2	2·58	2·1	1·35	2·58	2·96

We here have evidence that the microbes which are added to a phagocytic mixture to provide pabulum for the leucocytes operate upon these as vaccines. If further evidence of vaccines acting as leucocytic stimulins is required we have it in the subjoined table And this table further shows that the stimulin action exerted by vaccines is non-specific.

TABLE X.—COMPARISON OF THE PHAGOCYTIC INTAKE OF (A) LEUCOCYTES INCUBATED IN NORMAL SALT SOLUTION; AND (B) OF LEUCOCYTES INCUBATED IN NORMAL SALT SOLUTION CONTAINING GRADUATED QUANTA OF TUBERCULIN B.E.

The stimulin effect was judged of by the number of microbes ingested when the two kinds of leucocytes in question were incubated or centrifuged with a suspension of staphylococcus.

The figures for the different samples are expressed below as the ratios, the figure for the Control being arbitrarily represented as 1.

No. of Expt.	Length of incubation	Phagocytic efficiency of the leucocytes operating in plain normal saline taken as	Phagocytic efficiency of the leucocytes operating in normal saline containing B.E. in the following quantities: $\frac{1}{2M}$ to $\frac{1}{1{\cdot}5M}$	$\frac{1}{M}$ to $\frac{1}{0{\cdot}8M}$	$\frac{1}{600T}$ to $\frac{1}{400T}$	$\frac{1}{300T}$ to $\frac{1}{100T}$	$\frac{1}{100T}$ to $\frac{1}{10T}$	Above $\frac{1}{10T}$
1	9 minutes	1	–	–	–	–	17	–
2	35 minutes	1	1·5 ; 5·6	–	–	8·5 ; 1	–	1
3	60 minutes	1	2	–	3·1	3·7	–	–
4	Not noted	1	–	–	–	12	24 ; 24	–
5	20 minutes	1	4·6 ; 4	10	3	1	–	–
6	60 minutes	1	–	–	2·5	–	–	–
7	immediate centrifuging	1	11	17	–	–	–	–
8	1 hr. 45 min.	1	–	–	–	3	2	5 ; 10
9	30 minutes	1	5 ; 6	15	18	–	–	–

M = 1 millionth, T = 1 thousandth of a tuberculin suspension containing 1 mg. per c.c. of powdered tubercle bacilli.

Where the two separate figures appear in a single column of the table these indicate that I was here dealing with two specimens of blood which fell within the particular rubric.

We have still to consider more than one other class of stimulins. Among these there have to be considered drugs. And the drugs which especially invite examinations are the sulphanilamides. I have made experiments with one of these—M & B 693.

The results obtained are set out in the next table.

TABLE XI.—SHOWING THE PHAGOCYTIC COUNTS OBTAINED WITH NORMAL BLOOD, SERUM, AND CORPUSCLES, AND THOSE OBTAINED WITH THE SAME BLOOD, SERUM OR CORPUSCLES, INCUBATED WITH "693"; TOGETHER WITH (THESE BEING ADDED FOR THE SAKE OF COMPARISON) THE PHAGOCYTIC COUNTS OBTAINED WITH SERUM, BLOOD OR CORPUSCLES TREATED WITH VACCINES.

Serial No. of Experiment	Length of time during which the drug or vaccine operated upon the blood	Amount of the drug or of the vaccine which was added to the different blood specimens Blood specimen No. 1	Blood specimen No. 2	Blood specimen No. 3	Phagocytic indices of blood specimens No. 1	No. 2	No. 3	Procedures by which the figures here recorded were obtained
Expt. 1	75 minutes	Nil	$\frac{693}{10000}$	$\frac{B.E.}{500000}$	1	1·3	1·4	Procedure 1
Expt. 2	30 minutes	,,	,,	–	1	1·8	–	,, 1
		,,	,,	–	1	2·5	–	,, 2
		,,	,,	–	1	0·7	–	,, 3
		,,	,,	–	1	2	–	,, 4
Expt. 3	40 minutes	Nil	,,	,,	1	1	1·6	,, 1
		,,	,,	,,	1	1·4	1·7	,, 3
		,,	,,	,,	1	1·4	1·2	,, 4
Expt. 4	30 minutes	,,	,,	3,300 Staph. per c.c.	1	1·2	1·4	,, 1
		,,	,,	,,	1	1·6	1·5	,, 3
		,,	,,	,,	1	2·1	1·1	,, 4
Expt. 5	33 minutes	,,	,,	10,000 Staph. per c.c.	1	1·2	1·4	,, 1
		,,	,,	,,	1	1·6	1·7	,, 3
		,,	,,	,,	1	1·3	2·4	,, 4
Expt. 6	30 minutes	,,	,,	$\frac{B.E.}{500000}$	1	0·9	1·3	,, 1
		,,	,,	,,	1	0·8	0·6	,, 2
		,,	,,	,,	1	1	–	,, 3
		,,	,,	,,	1	1·3	1·1	,, 4

Procedure 1 : The separated washed corpuscles of the different samples of blood were incubated for fifteen minutes with normal serum and staphylococci suspended in normal saline.

Procedure 2 : The separated sera of the bloods were incubated for fifteen minutes with normal washed corpuscles and staphylococci.

Procedure 3 : The sera were incubated for fifteen minutes with staphylococci suspended in normal saline, and then after normal washed corpuscles had been added to the sero-microbic mixture, the completed phagocytic mixtures were incubated for another fifteen minutes.

Procedure 4 : The sera were incubated for fifteen minutes with washed normal corpuscles and after staphylococci had been added to the sero-corpuscular mixture the completed phagocytic mixture was incubated for another fifteen minutes.

Epitome of the data set out in the foregoing table.

It will be seen on study of the table that $\frac{1}{10000}$ of M & B 693 operates upon the leucocytes as a stimulin—we may call such stimulins "*pharmaco-stimulins*"—and that it increases their phagocytic avidity in the ratio of 1 : 1·4 (this being the average of six experiments); and sometimes as much as 1 : 2·5. This result compares with an average stimulin effect of 1 : 1·27 obtained under the same conditions with blood inoculated with $\frac{1}{500000}$ B.E.; and 1·3 for blood inoculated with 3,300 staphylococci per c.c.

Going back now to Tables IX, X and XI it will be seen that we have had demonstration in these of three different kinds of stimulins: in IX of *stimulins produced by heating serum*; in X of *bacterial stimulins*; and in XI of both these and of *pharmaco-stimulins*. To these may now be added a fourth kind of stimulins—those which can be extracted from leucocytes by incubating them in normal salt solution. These may be conveniently called *endo-leucocytic stimulins*.

I shall discuss these stimulins on another occasion for there are certain points more relevant to our subject matter which still require to be considered. The first of these is:

POSSIBLE BEARING OF THE FACTS IN TABLES IX, X AND XI ON THE TREATMENT OF BACTERIAL INFECTIONS IN WOUNDS

In the researches on the infections of granulating wounds which were carried out during the last war by my fellow-worker Prof. A. Fleming, striking results were obtained by making impression preparations from wound surfaces which had been untreated for some hours. The cover-glasses which were used for making the specimens were then immediately turned down upon agar plates, and were then incubated.

Here the ordinary result was for fairly numerous colonies—for the most part colonies of staphylococci and streptococci—to grow out under the cover-glasses wherever there were any vacant spaces between the blobs of pus.

And when impression preparations were taken from a wound after it had been carefully washed, leucocytes were here, as is natural, entirely wanting; but the bacerial colonies were now more numerous than before for the microbes could now, in the absence of leucocytes, grow out unrestrained.

When specimens were taken a little later, and freshly emigrated leucocytes had occupied the surface of the wound there were only few, and in many cases no surviving microbes.

And finally after a considerable interval of time microbic colonies again grew out in the impression preparations in the interspaces between the blobs of pus—this showing that the sterilization of the wound by the leucocytes had been somewhere or other left incomplete.

The important point is that when the corrupted discharges have been carefully removed from the wound surface, and this is maintained in a condition favourable to the emigration of leucocytes and to their bactericidal action, the wound is so nearly sterilized that only a slight reinforcement of the bactericidal forces already in action would seem to be required to effect complete sterilization.

Now that reinforcement might possibly, as the results set out in Tables IX, X, and XI show, be supplied by a local application of a leucocytic stimulin either in the form of a sulphanilamide or a bacterial vaccine.

The local application of sulphanilamide has of course become the routine treatment of bacterial infections of wounds.

But we do not know whether the drug should be employed in the strength which gives the most effective specific bactericidal action, or in the strength which gives the best results as a non-specific leucocytic stimulin.

That vaccines might also be employed in the treatment of bacterial infections of wounds would seem clear not only from the results set out in the tables just referred to, but also from *in vitro* experiments carried out as follows:

Two filter paper discs are taken and soaked—one in a very high dilution of a broth culture of staphylococcus (a watery dilution containing 1,000 to 3,000 staphylococci per c.c.); and the other in the same dilution of staphylococcus culture to which an appropriate dose of vaccine has been added.[1] Both discs are drained of all superfluous fluid and are then flooded with the same amount of defibrinated blood, or blood taken direct from the finger, and the discs are then covered in with cover-glasses and incubated for not less than 3 hours.

After that the paper discs are taken from under the cover-glasses; the red blood corpuscles are dissolved in hot water; and the now decolorized discs are lightly stained with methylene blue. A comparison now shows that always fewer—and generally very many fewer—staphylococcus colonies have grown out in the vaccinated than in the control disc.

There is nothing fundamentally new in this result. For exactly the same result is obtained when an appropriate dose of vaccine is added to the outside blood instead of being added to the paper disc.

In the case where we put the vaccine into the paper disc we are doing the same experiment as we should be doing if we put vaccine into a patient's wound; and when we put the vaccine into surrounding blood we are doing the same experiment as we should be if we were applying the vaccine in the ordinary way.

Let me now as a preface to what I want to say about vaccines dwell for a moment on the, at first sight, paradoxical fact that the blood, when it is tested under conditions in which epi-phylactic response is excluded, has no staphylo-phylactic power; that is to say it kills either no staphylococci or at best a minimal number of these.

I have dealt with the facts which lead up to this conclusion (I think it is a conclusion which applies generally to all serophytes) in a series of three papers, the first two of which were published in 1902[2] and in 1915.[3]

In the *first* paper I showed that the *serum* exerts absolutely no bactericidal power upon the staphylococcus or streptococcus or the *M. melitensis* or the plague bacillus. In the *second* I emphasized the fact that the *serum* furnishes an ideal cultivation medium for the whole of septicæmia-producing or as I prefer to call them, *serophytic microbes*.

And finally I showed in a paper published in 1923[4] that the normal *whole blood* exerts upon the staphylococcus practically no bactericidal power; and that we can never, as we do when we are speaking of the typho-bactericidal power of the normal serum, say of the non-epiphylactic blood that it will kill a definite number of staphylococci or other serophytes.

My whole blood, for example, exerts no bactericidal power when it is implanted with minimal numbers of staphylococci. It *begins* to develop bactericidal power only when more than 200 staphylococci per cubic centimetre are implanted. And it develops its maximum bactericidal power when it is implanted with between 4,000 and 5,000 staphylococci per cubic centimetre.

I have called that the *Caput and Cauda phenomenon* because when the figures for bactericidal power achieved by graduated doses of vaccine are set out in the form of a table we find that the percentage of microbes killed in the more heavily implanted bloods which occupy the head or caput of the table is always much greater than those for the lightly implanted bloods which occupy the whole tail of the cauda of the table.

[1] I have always used a vaccine consisting of $\frac{1}{1000000}$ dilution of B.E. suspension which contained 1 mg. of desiccated tubercle.

[2] *Journal of Hygiene*, 1902, **2**, No. 4 (reprinted in the Author's "Studies on Immunisation", Constable).

[3] *Proc. Roy. Soc. Med.*, October 8, 1915.

[4] *Lancet*, February 24, 1923, p. 368.

This fact that the blood, which had originally none, develops a bactericidal power to staphylococcus under the stimulus of a sufficient bacterial implantation, furnishes, as we shall see later, a possible explanation of the fact that the effects of prophylactic inoculation persist long after the manifest blood changes have passed off.

From that I pass to put before you certain general considerations about vaccines. Let me deal first with the question of dosage.

DOSAGE OF BACTERIAL VACCINES

An all-important first principle to appreciate in connexion with the testing of the phagocytic power developed in the blood by vaccines applied therapeutically *in vivo* or *in vitro* is that the phagocytic intake is never a simple function of the strength of the vaccine brought into application. Epiphylactic response is powerfully affected (this comes out with special clearness when we measure the phagocytic response to a vaccine implanted into blood *in vitro*) by the larger or smaller number of microbes we employ as "*phagocytic pabulum*".

The smaller the number of microbes employed as "pabulum" the larger is the dose of vaccine required to give a maximal epiphylactic response. And the larger the number of microbes employed as phagocytic pabulum the smaller is the quantum of vaccine required to give the same measure of response. In other words the principle of dosage which has to be borne in mind is that the epiphylactic ictus brought to bear upon the leucocytes is always composed of two or three factors—two in the case of blood inoculated *in vitro* (*one* being the microbes supplied to serve as a phagocytic pabulum, and *the other* the amount of vaccine superadded); and three in the case where an infected patient is inoculated (the *first* being the number of microbes harboured in his body; the *second* being the dose of vaccine administered; and the *third* being, when his phagocytosis is being tested, the phagocytic pabulum employed in the test).

The influence of the different amounts of staphylococcic pabulum employed in the phagocytic tests comes out clearly in Table X. The quantitatively different epiphylactic responses there recorded in different experiments in which one and the same dose of tubercle vaccine was employed would seem to be due to the different strengths of bacterial pabulum used in the different experiments.

Experiments made *ad hoc* bring confirmation of the principle in question. In the experiments set out below equal samples of my defibrinated blood were incubated with two different doses of Tuberculin B.E. vaccine there being, in the two sets of experiments, added to the phagocytic mixtures by way of pabulum the same quanta of staphylococcus culture.

TABLE XII.

Serial No. of expt.	Composition of Phagocytic mixtures employed	Phagocytic index of the vaccinated blood
1	2 vols. blood inoculated with $\frac{\text{B.E.}}{\text{1M.}}$ per c.c. + 1 vol. $\frac{\text{Staph.}}{5}$	1·7
	2 vols. blood inoculated with $\frac{\text{B.E.}}{\text{1M.}}$ per c.c. + 1 vol. $\frac{\text{Staph.}}{4}$	1·8
	2 vols. blood inoculated with $\frac{\text{B.E.}}{\text{1M.}}$ per c.c. + 1 vol. $\frac{\text{Staph.}}{3}$	1·1
	2 vols. blood inoculated with $\frac{\text{B.E.}}{\text{1M.}}$ per c.c. + 1 vol. $\frac{\text{Staph.}}{2}$	1·2
2	2 vols. blood inoculated with $\frac{\text{B.E.}}{\text{2M.}}$ per c.c. + 1 vol. $\frac{\text{Staph.}}{16}$	1·0
	2 vols. blood inoculated with $\frac{\text{B.E.}}{\text{2M.}}$ per c.c. + 1 vol. $\frac{\text{Staph.}}{8}$	1·1
	2 vols. blood inoculated with $\frac{\text{B.E.}}{\text{2M.}}$ per c.c. + 1 vol. $\frac{\text{Staph.}}{4}$	1·1
	2 vols. blood inoculated with $\frac{\text{B.E.}}{\text{2M.}}$ per c.c. + 1 vol. $\frac{\text{Staph.}}{2}$	1·5

We have in this, and the previous tables, the answer to the question of dosage which should, when treating a patient by vaccine therapy, be kept constantly in mind. These tables show that the initial dose of vaccine to be administered to an infected patient must always be a matter of clinical judgment—the heavier the patient's infection the smaller should be the amount of vaccine given for a first inoculation. And the rule for subsequent inoculations is this: When the first dose is adjudged to have been operative and to have exerted a favourable result, and when we have good reason to think (but never before) that the population of microbes in the patient's body has been reduced, we may correspondingly increase the dose of vaccine administered. And when the infection is very nearly extinguished we may use a dose of vaccine little less than that which would be administered for prophylaxis to a healthy man.

QUESTION AS TO WHETHER BACTERIAL VACCINES OPERATE SPECIFICALLY OR NON-SPECIFICALLY

As the terms "specific" and "non-specific" carry different meanings for different persons it will be necessary to begin by saying something about the terminology.

If only the single strain of microbes out of which the vaccine has been manufactured is killed or impeded in its growth by the vaccine inoculated the effect of the inoculation would be *specific in the narrowest sense*, i.e. type or strain-specific. If on the other hand the bacterial vaccine operates upon all microbes which are "*homonymous*" with that from which the vaccine was made the effect would be *non-specific in the sense which the term is customarily used.* And if, in addition to homonymic, heteronymic microbes are killed or are impeded in their growth by the vaccine inoculated, the immunizing effect exerted would be *non-specific in the widest sense.*

Homonymous microbes would be those which are called by the same name because they have similar cultural characters; produce similar clinical symptoms; manufacture similar chemical products; generate, when used as vaccines similar epiphylactic elements; and have, subject to the qualification below, similar chemical susceptibilities.

It is necessary to appreciate that when microbes which are called by the same name are found to differ in any cultural, clinical or immunological character; and also when they have been found to produce different chemical products; and to have different chemical susceptibilities; they can by the aforesaid criteria be distinguished into *sub-species*, or *types*, or *variants* or strains which finally receive distinguishing appellations of some sort.

There have in this way been differentiated—and this concerns the specific action of vaccines, the human, bovine, avian and reptilian strains of tubercle bacillus; and the sub-species or variants of the typhoid bacillus which are known as paratyphoid A and paratyphoid B.

Heteronymous microbes would be microbes which are called by different names because they have different cultural characters, produce different clinical symptoms, and different immunological responses; and have—this being subject to the reservation now to be made—different chemical susceptibilities.

Susceptibility or insusceptibility to one particular reagent cannot be regarded as a trustworthy criterion of generic affinity or lack of such affinity. This comes out clearly in the fact that M & B 693 operates with conspicuous effect only upon one particular strain of streptococci, while it operates also upon microbes as generally distinct as the meningococcus and the pneumococcus.

And further proof that the susceptibility or insusceptibility to one particular reagent is not of classificatory importance, is furnished by the fact that it is possible to breed out so-called "arsenic-fast" types of trypanosomes which do not as far as it is known differ from unmodified trypanosomes except only in the matter of being resistant to one particular arsenical.

These points of terminology having been made clear it will be seen that the question as to whether bacterial vaccines operate specifically or non-specifically resolves itself into three different questions.

(1) Do the bacteriotropic substances which are produced by and any stimulins which are set free in the body in response to the inoculation of a bacterial vaccine give protection only against microbes which are culturally, clinically, chemically and immunologically indistinguishable?

(2) Do these substances protect not only against the microbes which constitute the prime target of inoculation, but in addition against microbes which have slightly different cultural, clinical and immunological properties, but would be included under one and the same microbic species?

(3) Do the substances in question operate not only upon *homonymous* but also upon *heteronymous* microbes?

To the *first question* a definite answer is given in the fact that prophylactic inoculation —I limit myself for the moment to anti-typhoid and anti-cholera vaccination—would seem to be everywhere effective, i.e. effective upon all the different strains or varieties of typhoid and cholera which exist. And we have striking confirmation of this applying generally in the fact that vaccine therapy with stock vaccines is—at any rate in the majority of cases—as effective as treatment with autogenous vaccines.

With regard to the *second question*, a unique opportunity for deciding whether a bacterial inoculation is specific in the narrowest sense, or whether it protects also against homonymous microbes of different kinds, presented itself in the 1914-18 war. For there then offered themselves for observation: a large population of soldiers who were inoculated (in the early years of the war) with a simple typhoid vaccine; and side by side with these a large population of soldiers who were (in the later years of the war inoculated with a typhoid vaccine in conjunction with a paratyphoid A and a paratyphoid B vaccine.

That statistical opportunity was missed because it was thought necessary to add to the typhoid vaccine, without reducing the dose of that vaccine, half as much paratyphoid A vaccine and half as much paratyphoid B vaccine—this of course resulting in the second population of soldiers being inoculated with double the number of microbes given to the first population.

And at any rate the question under investigation remains unresolved for the statistics which were collected showed that there was no significant difference between the number of cases of paratyphoid A and B in the two populations.

And further evidence pointing to non-type specific immunization is furnished by the favourable prophylactic results against pneumococcus which were obtained by myself and my fellow-workers in the Transvaal with vaccines made with untyped pneumococcus.

The very striking results in question are set forth in a series of papers which were published in the *Lancet* in 1912 and were republished in book form.[1]

Facts which would seem to conduct to a directly contradictory conclusion have been put on record by many—chiefly American—investigators.

The experiments of these investigators would seem to indicate that animals which are inoculated with one particular strain of pneumococccus are protected only against that particular strain. But these, being purely statistical experiments have, like all such experiments, the vice of taking cognizance of only one particular effect—in this case *survival or non-survival after inoculation with supra-lethal doses.* And when this is borne in mind it becomes plain that all the statistical results I am referring to really establish is that better protection is given against the strain of pneumococcus which was employed as a vaccine than against other strains.

And what we have to settle before we call a pneumococcus type-specific or non-type-specific is *how much* protection is afforded against "homologous" and how much against "heterologous" strains.

Again most of the facts which are relied upon as proof of non-specific response to pneumococci are results obtained by serum therapy on animals and man. And there is, as we shall see in a moment, great difficulty in referring the favourable results obtained by pneumococcic serum-therapy to the administration of epiphylactic substances elaborated in the organism of the donor animal.

[1] "On Pharmacotherapy and Preventive Inoculation applied to Pneumonia in the African Native". Constable, 1914.

The *third issue* as to whether bacterial vaccines can, or cannot, afford protection against heteronymous microbes, can be put to the test in a number of different ways.

We have already in this connexion considered the observations which were made by Shattock and Dudgeon on the one hand, and by (Table IV *supra*) Dr. Ronald Hare on the other.

And what looks like clear statistical evidence of the protective effect exerted by a vaccine on heteronymous microbes is that set out in the following table, which shows the results obtained by pneumococcal vaccination in the Premier Mines in the Transvaal in 1911.

TABLE XIII.—SHOWING FOR THE WHOLE NATIVE POPULATION OF THE PREMIER MINE THE INCIDENCE AND DEATH-RATE FOR PNEUMONIA; THE INCIDENCE AND DEATH-RATE FOR "OTHER DISEASES"; AND ALSO THE NUMBER OF WORKING DAYS LOST THROUGH ILLNESS; FOR THE MONTHS OF FEBRUARY TO MAY, IN 1911, 1912, AND 1913 RESPECTIVELY.

	1911	1912	1913
Population (daily average strength)	10,426	12,549	15,284
Proportion of the population inoculated	0	About 50%	About 92%
Incidence-rate of pneumonia	4%	1·28%*	0·74%*
Death-rate from pneumonia	0·97%	0·31%	0·14%
Incidence-rate of other diseases	31%	20·7%	14·4%
Death-rate from other diseases	0·51%	0·38%	0·34%
Number of working days lost per 100 native labourers	275	177	131

* In 1912 the incidence-rate was 0·86% for the inoculated, and 1·7% for the uninoculated. In 1913 it was 0·6% for the inoculated, and 3% for the controls.

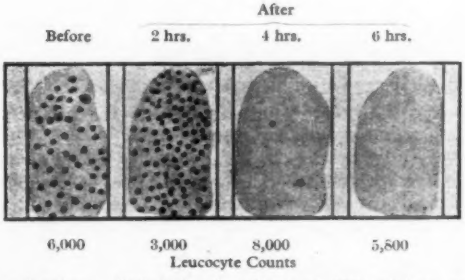
Further, convincing clinical evidence of the non-specific effect of vaccines is available in the fact that the intra-vascular inoculation of typhoid and coliform vaccines has proved itself an effective treatment for many different infections.

In particular it is credited with having given strikingly favourable results in gonococcal infections.

That these results find their most natural explanation in a non-specific immunizing response and not in a newly-invented type of reaction which has been christened "Protein Shock," will not be doubtful to anyone who has, from laboratory experimentation, learned to expect non-specific immunization *in vitro*.

Passing now from clinical to clinico-laboratory experiment I may lay stress on an experiment I published ten years ago. This showed that an intravenous inoculation of coliform vaccine first markedly diminished the staphylo-bactericidal power of the patient's blood and then formidably increased it.

FIG. 3.



Non-specific Immunization. Epiphylactic effect of 200 million coli vaccine administered intravenously. Tested in a slide cell by implanting the same number of staphylococci into each of the four successive 50 c.mm. volumes of blood.

The first sample of the patient's blood, taken before inoculation, killed off (*see* fig. 3) all except some 50 of the implanted staphylococci. In the second sample drawn two hours after inoculation, about double that number of staphylococci grew out into colonies. The third sample, drawn two hours after that killed all but two of the staphylococci implanted. And the fourth and last sample of blood, drawn from the patient six hours after inoculation, killed all the implanted and might easily, if it had been tested higher, have killed many more.

Non-specific epiphylactic responses of that sort are obtained whenever blood which has been inoculated with vaccine *in vitro* is tested by hæmo-bactericidal methods, i.e. by the slide cell or the capillary clot methods.

HAS CONVINCING PROOF OF ANY PURELY SPECIFIC IMMUNIZATION EVER BEEN BROUGHT FORWARD?

I shall confine myself to my own work and that of my fellow-workers. To test the specificity of the response to typhoid vaccine, I took the sera of six laboratory workers who had been inoculated against typhoid and tested their bactericidal power both to cholera and typhoid. I found in these experiments that the sera I was dealing with showed a greatly increased bactericidal effect to typhoid but no increased bactericidal power to cholera. I inferred from that that bacterial vaccines produce only specific epiphylactic effects. But in coming to this conclusion I had neglected to think of the leucocytes.

I may instance the further fact that when my fellow-worker, Dr. John Freeman, massaged a gonococcal knee with a view to determining whether the auto-inoculation produced would have a specific or non-specific effect, he found[1] that it markedly increased the phago-incitor power of the serum to gonococcus, but left the phago-incitor power of the serum to the tubercle bacillus quite uninfluenced.

Here again we all in my laboratory, quite forgetting that a different result might have been obtained if the leucocytes had been tested, rashly assumed that auto-inoculations operate only upon homonymous microbes.

Finally coming back to the fact that we get, as pointed out above, better results by testing leucocytic than by testing serum response, I may draw attention to the fact that when my colleagues and I were working on the pneumonia which was then epidemic in the Transvaal mines, we very laboriously searched for evidence of immunizing response to pneumococcus in the sera of ourselves, of healthy natives, and of natives who were suffering with pneumonia, and also of healthy natives inoculated with pneumococcus vaccine. We did this in order to test the effects of vaccine therapy, and also to choose a proper dose of vaccine for prophylactic inoculation. And the upshot of all this work was that satisfying evidence of the development of either increased bactericidal or phago-incitor power in the serum was conspicuously lacking.

The results obtained in our thousands of phago-incitor tests are too complicated to set forth here but the bactericidal results of our large numbers of serum tests are shown in Table XIV.

TABLE XIV.—SHOWING THE RESULTS OBTAINED BY TESTING THE PNEUMO-BACTERICIDAL POWER OF THE SERA OF FOUR LARGE GROUPS OF PERSONS.

Source from which the sera were derived	Total number of observations	Number of observations in which no microbes were killed by the serum	Cases in which 10-30 pneumococci were killed by 50 c.mm. of serum	Cases in which 30-90 pneumococci were killed by 50 c.mm. of serum	Average number of pneumococci killed by 50 c.mm. of serum from the group
Healthy Europeans	41	36	4	1	2 (approx.)
Healthy tropical natives	27	19	8	0	4 (approx.)
Tropical natives after inoculation with pneumococcus vaccine	176	161	15	0	1 (approx.)
Natives suffering from pneumonia	20	11	9	0	5 (approx.)

[1] Studies in Connexion with Therapeutic Immunisation, *Lancet*, November 2, 1907. (Reprinted in the Author's "Studies on Immunisation", p. 425, Constable, 1909).

And the very startling negative or practically negative results here recorded may be usefully contrasted with the fact that when at a later date the bloods of normal Europeans were tested by hæmo-bactericidal methods (i.e. slide cell or capillary clot methods) they gave instead of the small figures recorded above, figures of 50,000 and over of pneumococci killed per 50 c.mm. of blood.

The data in Table XIV suggest that the current interpretation of the favourable results of pneumococcal serum therapy may not be the right one. For if the sera of auto-inoculating pneumonic patients, and healthy men inoculated with pneumococcus vaccine, contain no bactericidal and seemingly no increased phago-incitor substances, it becomes difficult to believe that the sera of inoculated animals contain such substances.

IS THE ACCREDITED INTERPRETATION OF THE GOOD RESULTS OBTAINED WITH SERUM-THERAPY OF PNEUMONIA THE ONLY POSSIBLE ONE?

There are two other possible interpretations of the recorded facts. The first is that antigens, possibly antigens which act as stimulins, may be contained in the pneumococcal serum administered. This general possibility has already been considered in connexion with Neufeld and Rimpau's reported thermostable phago-incitor substances.

And the second possible explanation of the favourable results obtained in human serum therapy is that the processes of concentration and re-solution which have been applied to the serum administered to man may have converted these sera into stimulins. Many of the results which I have obtained with re-constituted sera seem to suggest that.

One is driven to this desperate resource of guessing at the explanation of the favourable results of pneumonic serum therapy by the fact there would seem never to have been any proper evaluation of the epiphylactic power of the anti-pneumococcus sera administered, or any proper evaluation of the blood of the patients before and after the administration of the serum.

PERSISTENCE OF THE PROTECTIVE EFFECTS OF PROPHYLACTIC VACCINATION

Everyone who has considered the evanescence of the increased bactericidal power which is achieved by antityphoid inoculation is agreed that the persistent specific immunization which is achieved must be due to some of the cells of the body remaining, long after all constitutional effects of inoculation have passed off, sensitive to re-immunization by such minimal typhoid inoculations as would inevitably occur in patients who were living in places where they are from time to time exposed to typhoid infection.

What cells in the body perform this work of re-immunization to typhoid is one of he important unresolved questions of bacteriology.

It may quite well be that it is the leucocytes which respond to infection; for that is not precluded by the fact that it is confidently asserted that that function is performed either by fixed cells distributed all over the body, or by fixed cells closely associated with the blood, and the ascription of this function to the leucocytes would at any rate harmonize with the fact that extravascular blood that possesses either none or only minimal staphylo-bactericidal power acquires when inoculated plentiful bactericidal power.

Further, it looks as if the question could easily be settled by direct experiment. It would be perfectly easy to take a series of samples of blood of patients who have been inoculated with typhoid (the taking of the first of these samples being deferred until the constitutional disturbance produced by the inoculation has died down) and to compare (using for this purpose very small doses of typhoid vaccine) the sensitiveness of the leucocytes of these bloods with that of the leucocytes of normal bloods.

If I were not too far "declined into the vale of years", and if I had not more important matters to investigate, I should myself undertake such a series of experiments. As things are I commend the suggested procedure to younger research workers.

Finally I subjoin, by way of a key to the reasoning in this paper, the following tables:

TABLE A.—PASTEURIAN DOCTRINE OF IMMUNIZATION

(This was based on what was known or believed to hold true of Jennerian vaccination; and it constituted the foundation of all the Pasteurian extensions of that system of immunization.)

(1) Immunization can be undertaken whenever the pathogenic microbe of a disease has been isolated, or when material which contains that microbe is available.

(2) It is a *sine qua non* for successful vaccination that it should be carried out with living microbes.

(3) Immunity is established only after the expiration of ten days.

(4) Immunization is practicable only in advance of the infection—with a possible exception in the case of any disease in which the incubation period lasts sufficiently long for immunization to be completed before the symptoms of the disease become manifest.

(5) The amount of vaccine which is administered need not be minutely regulated. All that is required is to make sure that the microbe which is employed has been adequately and permanently attenuated.

(6) Success or failure of an immunization procedure can be judged only by statistical methods.

That involves in the case of animals, inoculating them and their controls with a virulent culture of the specific microbe of the disease. And it involves in the case of man the registering of the incidence and death-rates of formidable numbers of vaccinated persons and controls who have been equally exposed to the infection against which it is hoped to give protection.

CONTRARY GENERALIZATIONS ENUNCIATED BY THE AUTHOR IN PAPERS PUBLISHED BETWEEN 1897 AND 1901

(1) Inoculations can be successfully carried out with sterilized vaccines.

The fact that agglutinins are elaborated in response to bacterial inoculations has been previously shown by Richard Pfeiffer.[1]

(2) An increase in the bactericidal powers of the blood can be registered very shortly; to wit, within one day or less after vaccination.[2]

(3) Vaccines can be employed not only prophylactically but also therapeutically in the treatment of infected patients; and here the phagocytic power of the blood is very rapidly increased.[3]

(4) The measure of immunity conferred by an inoculation procedure can be gauged by measuring the changes effected in the bactericidal and phagocytic power of the blood.

[1] *Wright and Semple*—"*On vaccination against Typhoid Fever*", Brit. M. J., *January* 30, 1897.
Wright and Leishman—"*On the Results which have been Obtained by the Anti-typhoid Inoculations, and on the Methods which have been Employed in the Preparation of the Vaccine*", Brit. M. J., *January* 20, 1900.

[2] *Wright*—"*On the Changes Effected by Anti-typhoid Inoculations in the Bactericidal Power of the Blood, with Remarks on the Probable Significance of these Changes*, Lancet, *September* 14, 1901.

[3] *Wright*—"*Notes on the Treatment of Furunculosis, Sycosis and Acne by the Inoculation of a Staphylococcus Vaccine, and Generally on the Treatment of Localized Bacterial Invasions by Therapeutic Inoculations of the Corresponding Bacterial Vaccines*", Lancet, *March* 29, 1901.

Table B.—Dealing with the Machinery of Immunization.

Rival Doctrines dating from 1890 or before.

Humoral Theory.—Immunization consists in the elaboration of bactericidal substances and in the conveyance of these into the blood-stream.

Phagocytic Doctrine of Metchnikoff.—Immunization consists in training the leucocytes to confront and phagocytose the specific pathogenic microbes against which the animal has been inoculated.

Doctrine of the author with regard to the machinery of immunization set out in papers published between 1897 and 1908	Logical grounds which were felt to justify the conclusions set out in column 1	Revision in the light of new data of the doctrine set out in column 1
(1) Phagocytosis of microbes takes place only in the presence of serum	When leucocytes have been washed free from serum phagocytosis of microbes is abolished	*Vide* new data set out in Tables VI, VII, and VIII, pp. 14 and 15.
(2) The chemical reaction which takes place in a phagocytic mixture (i.e. mixture of corpuscles, serum and microbes) is an opsonic action	Of the three *a priori* possibilities (1) that the serum acts opsonically on the microbes; (2) that the serum may function as a leucocytic stimulin; and (3) that the microbes which are added as phagocytic pabulum may vaccinate the leucocytes; only the first appears to be admissible	*Vide* new data showing that the microbes which are contained in a phagocytic mixture operate as a vaccine on the leucocytes of that mixture (*vide* Table IX, p. 15) and that a serum may exert a stimulin effect on the leucocytes. *Vide* Table V, Sects. 1 and 2, p. 13.
(3) Serum is rendered inert by heating to 60° C.—this result being due to the destruction of the opsonins	Comparison of the effects of heated serum with that of unheated serum (*Vide* Table V, Sect. 1, p. 13)	*Vide* new data set out in Table V, Sect. 2, p. 13.
(4) Immunizing response of the patient to the inoculation of bacterial vaccines affects his serum and leaves his leucocytes unchanged	*Vide* Chiastic Experiments, *Proc. Roy. Soc.*, **73**, 1903, and **74**, 1904, republished in the Author's "Studies on Immunisation", pp. 87, 90 and 117.	*Vide* new data set out in Chiastic Table III, p. 12.
(5) The whole of the increased phagocytosis which is obtained by the inoculation of bacterial vaccines is to be ascribed to an elaboration of opsonins in the serum and not to an elaboration of leucocytic stimulins	This was inferred from Ehrlich's axiom that inoculations lead always to the elaboration of antithetic chemical substances, and as a corollary from that that bacterial vaccines lead to the elaboration of *bacteriotropic* as distinguished from *leucocytotropic* substances	*Vide* Tables X and XI for evidence of stimulin action exerted on leucocytes by bacterial vaccines, and also by M & B 693, pp. 16 and 17.
(6) Leucocytes kill microbes only intracellularly	*A priori* assumptions	Leucocytes can kill microbes extracellularly. *Vide* p. 9.
(7) The blood *in vitro* will not respond to inoculation	*A priori* assumptions	The blood does, when inoculated *in vitro*, exhibit increased bactericidal and phagocytic power, and does this often instantaneously; often in the course of a few minutes; and it would seem always in the course of two hours. *Vide* papers published by the Author*
(8) The anti-bacterial substances which are elaborated in the body in response to bacterial vaccines operate only on the kind or sort of microbes which have been inoculated	*Vide* Immunization Curve No. 53 originally published in the *Lancet*, November 2, 1907, and republished in the Author's "Studies on Immunisation" (Chart 44)	*Vide* results of prophylactic inoculation against pneumonia in the Transvaal: Table XIII, p. 22; and non-specific clinical effects of intravenous inoculations of vaccines; p. 22. *Vide* also direct laboratory experiments — in particular Slide Cell Experiment p. 22, fig. 3. Shattock and Dudgeon's results p. 13, and Dr. R. Hare's results, Table IV, p. 13, also inoculations on blood *in vitro*. *Vide* papers referred to on this page.*

* *Lancet*, March 29, 1919; February 24, 1923 (p. 365) and August 1, 1931 (p. 225); August 8 (p. 277); and August 15 (p. 333)

Clinical Section

President—G. DE BEC TURTLE, M.D.

[*November* 14, 1941]

Partial Thrombosis of the Right Internal Carotid at Level of Ophthalmic Artery, and Probably also a Thrombus in the Upper Dorsal Region of the Pons on Right Side.—WILFRED HARRIS, M.D.

M. B., male, aged 61. Has been professional pugilist, and has served in the Canadian Mounted Police, and in the Navy. Wounded by a bullet, right anterior parietal bone, in 1929, resulting in left hemiplegia. Decompressed, and recovered. Wounded at Dunkirk in May 1940, and given prophylactic antitetanic serum. Three months ago wounded in left shin on board ship.

September 21, 1941: Admitted to St. Mary's Hospital with well-marked tetanus, generalized twitchings, trismus, risus sardonicus, and opisthotonos when stimulated. Given 191,000 A.T.S. units intrathecally and intravenously. Rapid recovery, and in ten days was allowed up for walks. In mid-October, when in a shop near the hospital, sudden momentary faintness occurred, left leg dragged, and there was mistiness of right vision, which has increased. Tremor of head noticed since recovery from tetanus. Two days after the faint, right pupil observed to be widely dilated. Right vision fingers only. Cerebrospinal fluid pressure 210.

On examination.—Weakness of left arm and leg, but no rigidity or increase of deep reflexes; left plantar reflex: flexor. Well-marked left hemianæsthesia below angle of jaw, and also over right trigeminal area. Right vision still fingers only; colour of right disc definitely paler than left, with contracted central artery. Blood-pressure 200/100.

Present condition.—The colour of the right disc has improved to normal, and the central artery is nearly equal to the left. The vision remains unaltered in the right eye, with a contracted visual field.

The prism test demonstrated that the right amblyopia was functional, the ascertained visual acuity of the right eye being nearly equal to the left.

The functional amblyopia is probably due to auto-suggestion following a temporary occlusion of the arteria centralis retinæ.

Adie's Syndrome (Tonic Pupils).—HELEN DIMSDALE, M.R.C.P. (for WILFRED HARRIS, M.D.).

Female, married, aged 22, though feeling in perfect health, with no history of any illness beyond childish complaints, when applying in August 1941 for a post in an industrial firm in the suburbs, was refused by the doctor examining for the firm, who made the diagnosis of neurosyphilis.

On examination.—The pupils are unequal, the right pupil medium large, the left considerably smaller, resembling the Argyll-Robertson pupils in that neither reacts to light in the ordinary way, but, unlike the Argyll-Robertson pupil, contracting slowly to accommodation (tonic reaction).

After she has been in a dark room for half an hour, both pupils contract partially to a bright light. She states that she has known as long as she can remember that her pupils have been unequal. The ciliary muscles function normally, and the fundi and the optic discs are also normal. No ptosis.

The knee-jerks, Achilles and forearm-jerks are all absent. There is no ataxy, no Romberg sign. She denies having any pains in the limbs, and there is no sphincter disturbance.

The teeth are good, the upper central incisors being perfect. The blood Wassermann and Kahn tests were completely negative.

(Since the Meeting on November 14, the cerebrospinal fluid has been examined and found normal in all respects. Wassermann reaction and Kahn test, cells, protein, and colloidal gold test negative.)

Hyperpiesis with Polycystic Kidneys treated by Sympathectomy and Adrenal Gland Reduction.—A. DICKSON WRIGHT, M.S.

Mrs. B. S., aged 40, first seen in February 1939, referred by Dr. Wilfred Harris, complaining of:

Incessant throbbing, right-sided, occipital headache for four months requiring morphia and other drugs for its relief. Vertigo for a similar period; this symptom together with the headache had kept her more or less constantly in bed. Dyspnœa and angina pains for eighteen months. Epistaxis for four years. Five-minute attacks of hemi-paræsthesia during last four months.

On examination.—A pale hyperpietic woman, prematurely grey. Blood-pressure averaged 220/100. Heart enlarged, with duplicated second sound. The blood-pressure fell in sleep to 140/100 and under deep pentothal anæsthesia to 158/110. Examination of renal functions showed them to be depressed, and the blood urea was sometimes as high as 70, but the urine contained no albumin or casts. The eye grounds showed some venous nipping, silver wire arteries and blurring of the disc edges.

At the first operation on the left side (11.5.39) the kidney was discovered to be polycystic and about twice the normal size. One cyst at the upper pole was as large as a billiard ball. All the splanchnic nerves were excised with half the cœliac ganglion; the second and third lumbar ganglia were removed and half the suprarenal gland.

After operation the pressure fell to 145/100 and a week later rose to 165/110. The patient was so pleased with the improvement in her symptoms that she asked for the other side to be done and following this (15.6.39) the pressure became 105/65. The kidney on this side was polycystic like the other. Half the right suprarenal gland was removed.

On discharge on 3.7.39 the blood-pressure was 138 when standing and 154 when lying. Her headache was the last symptom to disappear, but now she is well and works in twenty-four hour shifts as a telephonist and has no hyperpietic symptoms two and a half years later.

COMMENT.—The possibility of the hyperpiesis being essential and not secondary to the polycystic kidneys is worth considering. The reason for showing this case is to draw

attention to the fact that if the kidney condition had been discovered before operation, sympathectomy would probably have been withheld, and so a very suitable case would have been left unaided. In the search for contra-indications it is possible to be too selective and cases which could be helped are sometimes left.

Dr. F. PARKES WEBER thought that the association of polycystic kidneys with hyperpiesia was only a coincidence, since extreme hyperpiesia was not usually a sign of polycystic kidneys until the terminal period, when operation would be hopeless.

Aneurysm of Circle of Willis.—A. DICKSON WRIGHT, M.S.

Mrs. M. S., aged 67. Since childhood has been troubled with migraines which were relieved by vomiting. They occurred only occasionally and were not localized.

About 1930 the headaches became more severe and were localized to the right frontal region "behind the eyes" and to the right face. Occasional vomiting.

May 1937: Attended hospital and was given "electrical treatment". During this treatment a right facial palsy developed which has persisted, and she also suffered occasionally from earache on the right side.

1939: Headache constant. Latterly she noticed the right eyelids opening "lazily".

6.10.41: Headache became almost unbearable, and this attack was preceded by vomiting. One week later the right eye closed. She occasionally felt dizzy during this last attack—had never felt so before.

About 14.10.41: Seen by Dr. Wilfred Harris who reported almost total 3rd nerve palsy, anosmia on right side, severe pain in first and second divisions of trigeminal nerve and slight reduction in sensation in the same area.

24.10.41: The right internal carotid was injected with thorotrast and an aneurysm the size and shape of a butter-bean was revealed. It was situated in the anterior part of the circle of Willis. The artery was immediately tied above the needle puncture just above the bifurcation of the common carotid.

After operation the foot of the bed was kept raised for a week, and the patient's position was very gradually altered until she sat up after three weeks. During this time ephedrine was administered (gr. ½ t.d.s.) and bellergal, the first to raise blood-pressure and the second to prevent arteriospasm.

The pain has practically gone, and the 3rd nerve palsy is rapidly disappearing.

Ulcerative Colitis Complicated by Polyarthritis treated by Total Colectomy.—A. DICKSON WRIGHT, M.S.

A. H. S., male, aged 31, first seen on May 8, 1938, with symptoms of ulcerative colitis. The diagnosis was confirmed by sigmoidoscopy and an appendicostomy was done. Yatren instillations resulted in great improvement, and the colitis settled down to a chronic state; X-rays showed stricture formation. Pyrexial arthritis developed and the large joints of the body and the spine were involved, the knees and the wrists being most affected. After consultation it was decided to remove the colon as no other focus of infection could be found.

This was done in one stage and the ileum was anastomosed to the recto-sigmoid junction; although without a colon, he now has one regular formed action every day. There are occasional attacks of proctitis with a little bleeding and mucus formation. The patient is much mutilated by the arthritis, but the disease has been quiescent since the colectomy and he is now having joint adhesions broken down under anæsthesia. He

recently had a laparotomy for a strangulation of the small intestine by a band, and this he negotiated satisfactorily.

Constrictive Pericarditis.—G. W. PICKERING, F.R.C.P.

Mrs. F. F., aged 46 years. Occupation: Home duties.

Past history.—Left pleurisy with effusion at 14 years of age; "rheumatic pains" in ankles and left shoulder for many years. No rheumatic fever, scarlet fever, tonsillitis or tuberculosis. Two miscarriages, 1921-22.

History: 1926: Complained of breathlessness and palpitations when walking on the level, but no swelling of ankles. Symptoms disappeared after three weeks' rest in bed.

1937: Again complained of breathlessness on slight exertion, and of a "puffed-out feeling" in epigastrium, but still no swelling of ankles. In hospital for three months and given digitalis. From then until November 1940 her only symptoms were breathlessness going upstairs and fullness after meals.

November 1940: Noticed that her navel was pushed out. This was relieved by rest at home.

February 1941: Admitted to hospital; abdomen tapped; given digitalis for three months and then discharged. May and June 1941: Given intravenous salyrgan 2 c.c. twice weekly, but with little effect. July 14, 1941: Seen in Out-patients' Department complaining of breathlessness and swollen abdomen. She had walked to hospital and was breathless but not grossly so.

On examination.—Gross ascites prevented the liver being felt; neck veins engorged to 6 in. above angle of Louis, but collapsing for brief moment in each cardiac cycle; forcible impulse in 5th left space 5 in. from mid-line, and pulsation in 4th left space just internal to impulse, and in 3rd left space near sternum. All these pulsations appeared to be systolic retraction. The right heart border was 2¼ in. from mid-line. No dullness in 2nd space, but dullness at inner end of 3rd left space. Heart rhythm regular. The second sound was reduplicated at the impulse and at the second left cartilage. Blood-pressure 108/90. No abnormal physical signs in lungs or central nervous system.

July 21, 1941: Admitted as in-patient. Ascites tapped on July 24 and 12 pints removed. This enabled the liver to be felt to 3 in. below the costal margin in the mammary line. It was firm and pulsating.

Throughout August venous pressure was 12-15 cm. above angle of Louis. Heart-rate 60-70. Fluid intake restricted to 30 oz.; daily urine output 10-20 oz. Tincture digitalis 60 ♏ per day for four days, then 45 ♏ for four days. It produced slowing to 36 beats per minute without diuresis, and was then stopped. Ascites tapped on August 30 (20 pints) and September 6.

Investigations.—X-rays, 26.7.41: "No evidence of pericardial calcification. Appreciable degree of ventricular hypertrophy apparent; vigorous hypertrophic type of pulsation of left ventricular origin." Blood urea, 29.7.41: 34 mg. per 100 c.c. Wassermann reaction negative. Urine: Sp. Gr. 1020-1024; always slight cloud albumin; occasional hyaline cast present. Blood, 29.7.41: Hb. 98%; C.I. 1·0. Electrocardiogram: Auricular fibrillation; low potential all leads. Vital capacity: 1,250 c.c.

Operation, September 8, 1941, under cyclopropane anæsthesia, in semi-recumbent position (Mr. A. Dickson Wright).

Mr. A. Dickson Wright: The operation was not especially difficult. A large pectoral flap was turned back and three chondral cartilages and the inner end of the ribs removed. There was no safe space between the pleural cavities so the left pleural cavity was opened. The heart was firmly encapsuled with fibrous pericardium and the two layers firmly fused together were dissected piecemeal from the surface of the heart. The right ventricle was slightly torn and had to be stitched. At the completion of the operation the heart seemed to be expanding freely in diastole. The convalescence was

straightforward and seemed to be greatly helped by a special oxygen mask, recommended by the anæsthetist, Dr. L. H. Morris.[1]

Post-operatively: A left pleural effusion developed to the level of the lower angle of the scapula. This slowly absorbed and had gone by October 17. Venous pressure 9 cm. four days after operation, and by October 17 it was varying from 5 to 7 cm. Abdomen tapped on September 11 (4½ pints) and on September 25 (10½ pints) since when it has remained undistended.

Post-operative electrocardiogram: Auricular fibrillation; greater potential in all leads than before.

Discharged 18.10.41. Patient now on 1 pint per day fluid intake; she has mersalyl 2 c.c. twice weekly. Urine output after mersalyl 70-90 oz. and about 20 oz. on intervening days. Now walks half a mile without dyspnœa.

[1] This mask was described by Barach and Eckman in *Anæsthesiology*, 2, No. 4, 421. In appearance it is similar to the B.L.B. mask, except that the respiratory bag is larger, and its capacity one gallon. By means of an injector attached to the oxygen regulator, the percentage of oxygen in the inspired air delivered to the patient is constant, irrespective of the rate of flow to the mask. The oxygen concentration can be varied between 40 to 100%, in ordinary use 40 to 60% is sufficient for the needs of most patients. No rebreathing occurs, thus the carbon dioxide percentage does not rise above 0·2 and no increased pressures are developed in the mask during respiration. This is obtained by the insertion of an inspiratory valve between the respiratory bag and the nose mask and a light expiratory valve placed on the mask opposite the nose. Control of the apparatus is simple, the rate of flow of the mixture is set so that the respiratory bag remains comfortably full, a flowmeter is not required. It is economical in use, a large 100 ft. oxygen cylinder lasts about sixteen hours. Drying up of the oral, nasal and pharyngeal mucous membranes, commonly met with in prolonged oxygen therapy, does not seem to occur, this is, no doubt, due to the fact that the injector draws in atmospheric air.

The mask was in continual use for eight days following the operation and gave definite relief to the patient. It is of interest to note that on the second night a delay occurred in changing the oxygen cylinders and as the patient became slightly delirious, a B.L.B. mask was substituted. This she did not tolerate for long, the original mask was restored to her and the anoxæmia was relieved.

This mask has three advantages over the B.L.B. mask: (1) The delivery of a constant proportion of oxygen and air irrespective of the rate of flow. (2) No increased pressures are developed during respiration. (3) No rebreathing and consequently no building up of carbon dioxide.

The mask was kindly lent by the Medical and Industrial Equipment Co., 12, New Cavendish Street, W.1.

Pulmonary Hypertension with Pulmonary Regurgitation Possibly due to Interatrial Septal Defect.—W. D. W. Brooks, D.M., F.R.C.P.

Mrs. T. G., Jewess, aged 40.

Family history not significant.

Personal history.—Hæmoptysis (varying in amount up to ½ pint) on five occasions since January 1939. Slight dyspnœa on exertion recently. Apart from occasional colds in the winter, she has had no illness of note.

Physical signs.—A well-built, rather stout woman, dyspnœic on slight exertion. Cyanosed; no clubbing of fingers and no evidence of congestive heart failure. Blood pressure, 125/80. The heart, however, is enlarged, beats regularly, and presents the clinical signs of pulmonary regurgitation. Râles are occasionally audible at the bases of the lungs. Nothing else abnormal.

Investigations.—Blood-count: R.B.C. 7,000,000; Hb. 131%; C.I. 0·93; W.B.C. 9,800. Sedimentation rate: 3 mm. (Westergren). Sputum: Tubercle bacilli absent (3 occasions); no significant infection. Urine: No abnormality found.

X-ray examination.—Lungs: Generalized gross vascular congestion. Heart: Increased in size due to enlargement of both ventricles; conus and pulmonary artery considerably

enlarged. Electrocardiogram: Slight right axis deviation, curves otherwise within normal limits.

Dr. PARKES WEBER said he thought that the pulmonary regurgitation was probably due to atheromatous disease of the pulmonary valve, which occasionally occurred when the valve was the site of a slight congenital (developmental) abnormality, for instance, two of the cusps being congenitally more or less fused together, the valve thus being a *locus minoris resistentiæ*.

Sclerodermia and Dermatomyositis.—C. G. BARNES, M.D.

Man, aged 66. Tongue became swollen and hard in October 1940 after dental extractions, and sclerodermia of the lips and cheeks developed. Legs became œdematous and painful, and dermatomyositis spread, involving the whole body except the chest. All the affected muscles were firm and tender, with contractures in the limbs. Sclerodactyly of hands without Raynaud's phenomenon or pigmentation. Afebrile, and no cardiac or renal lesion.

Oral aperture now becoming smaller, and face losing expression. Arms and hands greatly improved after treatment with thyroid extract and salyrgan, but trunk and limbs still greatly œdematous, and abdominal muscles board-like. Tongue very hard and almost immovable.

Investigations.—Urine, renal function, blood-count and cardiogram all normal. Wassermann reaction negative. No creatinuria. Basal metabolic rate: −14%. Plasma proteins 5·8 g./100 c.c. Albumin 4·0%, globulin 1·8 g.%.

Glucose tolerance curve: fasting 90 mg., ½ hr. 130 mg., 1 hr. 148 mg., 2 hr. 140 mg. per 100 c.c. after 50 g. of glucose.

[Sections of muscle removed at biopsy, and radiograms of soft tissues were shown.]

Dr. PARKES WEBER thought that the case was an extreme example of one type of dermatomyositis, namely, the type formerly known as the generalized symmetrical ("hypertrophic") form of sclerodermia. He knew of one case in which the general "puffy" appearance was at first so marked as superficially to resemble renal œdema.

DEMONSTRATION

Dr. J. Skládal (Prague) demonstrated a case showing expiratory reduplication sound which arises on auscultation when the author uses his method of a sudden expiration instead of provoked coughing (*See* "Pleuro-subpleural Zone", by J. Skládal, Cambridge University Press, 1942.) This has been found clinically to be a simple test for subpleural consolidation.

Section of Orthopædics

President—C. LAMBRINUDI, F.R.C.S.

[*October* 11, 1941]

MEETING HELD AT HORTON HOSPITAL

The Foot Problem in Service Cases

By H. L.-C. WOOD, M.S., F.R.C.S.

INTRODUCTION

DURING the last eighteen months we have seen a great number of foot cases referred for advice. We have tried to obtain the view-point of the Battalion Medical Officer by maintaining close touch through letters, interviews at the time of consultation, and by visits of my colleagues and myself to local units and training establishments. It has been our aim, by personal discussion, to see how best we can help.

Whereas in civil practice a major surgical procedure may be indicated for the relief of a certain foot condition, in circumstances of conscript military service the surgical condition and its treatment is largely subsidiary to the co-operation and willingness of the patient to become an efficient soldier. In other words, in an unwilling patient surgery may do more harm than good. For this reason I shall say little about the relief of major disabilities.

TYPES OF DISABILITY

In the terminology of the Medical Board Category Sheets, the foot troubles we encounter fall into three main groups:

(1) *Severe.*—Not remediable by operation to the extent of making an efficient soldier.
(*a*) Severe hallux rigidus and hallux valgus.
(*b*) Rigid flat feet.
(*c*) Severe claw foot.

I know that in a modern army men in this group can do useful work of a sedentary nature, but it is only recently that Medical Boards have been retaining their services for this purpose. We have been rightly advised not to operate on these conditions, but to submit the men for regrading or discharge, and our experience confirms this ruling.

(2) *Moderate disability.*—Remediable by operation.
(*a*) Hammer toe.
(*b*) Removal of exostoses, including the slicing operation for early hallux valgus.
(*c*) Amputation of fifth toes.
(*d*) Manipulations.

The only observation I would make upon this group is that when an arthrodesis for

hammer toe is done, the man should be hospitalized and the toe splinted for not less than six weeks. I have seen several who were not, with disastrous results to the arthrodesis.

(3) *Minor disabilities.*—Remediable without operation. This is the most important group and it includes:

(*a*) *Metatarsalgia* with flat anterior arch. (Most common of all.)
(*b*) Corns, callosities and verrucæ.
(*c*) Acute foot strain.
(*d*) Early degrees of flat foot.
(*e*) Moderate hallux valgus.
(*f*) Short tendo Achillis.
(*g*) Mild claw toe.
(*h*) That most intractable condition, epidermophytosis pedum.

This last is common, and is the source of much minor discomfort, but, although difficult to cure, it should be dealt with efficiently by the Battalion Medical Officer.

Perhaps I should add to the lengthy list the "malingering foot".

MINOR DISABILITIES

The first problem to tackle is how best these men can be treated.

This hospital is primarily a consultation centre to which men are sent for *advice,* and in some cases a note to the medical officer is all that is needed. It often happens that the medical officer does not want advice; the diagnosis is obvious; what he wants is *treatment for his patient.* It is not because he is incapable of carrying this out himself, but because no facilities exist for so doing. This is confirmed in conversation; nor do adequate facilities exist at the subsidiary E.M.S. hospitals of this Sector. For example, the only mechanism for obtaining an insole is to order one as a "surgical appliance," through the routine military channels. The same applies in a lesser degree when a boot is found to be too small and a refit is necessary.

I am sure that it is wrong to admit a man to hospital if out-patient treatment is possible. Once he is admitted, the hospital complex develops and cure is uncertain.

A solution has been found at Horton by the institution of an out-patient "foot clinic".

The working is as follows:

(1) General out-patient consultations are held twice weekly for all types of case.

(2) Foot cases are sorted into two groups: (*a*) Those needing *in-patient* treatment: (i) Remedial exercises; (ii) manipulation; (iii) operation. (*b*) Those who can be treated as out-patients.

(*a*) In particular the cases of acute foot strain benefit from a *short* period in hospital, but this should not exceed three weeks or the man will be unable to return to his unit, because of the operation of the "Y" list. This is undesirable and should be avoided, as it leads to convalescent depôts, and psychological complications.

(i) In regard to *remedial exercises,* there is no doubt that if these could be carried out under the supervision of the Unit Medical Officer, or at a nearby hospital, it would be ideal; but it is seldom possible to arrange this, and a short stay in hospital is the next best thing. While we aim at rapid restoration to normal, a further difficulty arises in that the man may have to wait for discharge after treatment is ended; and during this time his morale deteriorates and other disabilities appear.

The indications for operation and manipulation I have already touched upon.

(*b*) In the *out-patient group* are men with metatarsalgia, corns, flat foot, short tendo Achillis, &c., in other words, those men who can be benefited by *simple* expedients, such as the alteration of the size of boots, the provision of heel wedges, insoles, and metatarsal bars, or the attention of a chiropodist. These men are sent direct from the out-patient department to the "foot clinic".

Here, a routine method is adopted.

(i) The feet are measured in the weight-bearing position and the measurement checked against the size of boot.

(ii) Socks are inspected; the *shrunk* sock is apt to be forgotten as a cause of claw toes.

(iii) If wedges or insoles are needed, they can be made and fitted the same day.

The fitting of insoles and metatarsal bars must be personally checked by the surgeon, and adjustments made at the time. To facilitate this, the partly finished product is sent

to the clinic, and only returned to the cobbler for completion, after the fitting has been checked. Owing to the hard wear to which insoles are subjected, it is desirable to provide two pairs. The work is done by a cobbler, an ex-patient who was the victim of an air raid. It is cheap—for example, an insole with sponge-rubber metatarsal bar can be made for about ninepence.

Arrangements exist for similar clinics to be held at some of the outlying Sector hospitals, but at present the men have to attend here for the cobbling to be done. We hope to make some provision for this at these outlying hospitals, in order to save time and transport.

Follow-up.—The idea of a modern soldier going into battle wearing a valgus insole or a metatarsal bar, may seem ludicrous. When possible, we have followed up our cases and have established the fact that these men do get real benefit, and can return to full duty, often without need for lowering of category. There is usually a period of bitter complaint for ten days or a fortnight, but if the Unit Medical Officer will encourage the man to continue with his appliance it is found that he soon becomes comfortable and carries on.

Two practical points have emerged:

(1) The football bar or rocking bar used for hallux rigidus tends to wear out rapidly; consequently an inside sponge rubber bar is preferable. Studding the football bar with nails might be an alternative solution.

(2) The recommendation of civilian-type boots is seldom necessary. The army-type boot is excellent and with minor adjustments can be made comfortable. We find civilian shoes worn frequently, but their type and shape are usually unsuitable, and, also, it is against the Regulations.

Regrading for minor foot disabilities.—To lower a man's category is demoralizing. So-called "light" work in the Army would be heavy work to some of us, and may consist of fatigue duties, or prolonged standing in a cook-house. The disability remains unremedied and unrelieved. Hence we avoid regrading where possible.

SUMMARY

We wish to build up an organization in the Sector which will give a rapid and efficient service to Unit Medical Officers stationed in the locality of our outlying hospitals. This service to consist of:

(1) Advice. (2) The provision of simple appliances. (3) Remedial treatment under the direction of competent physiotherapists. To this end, the establishment of "local" foot clinics, complete with a chiropodist, cobbler, and physiotherapist is desirable.

In addition, a rapid means of obtaining boot refits must be worked out in connection with the Army authorities. For instance, at the large centres a small stock of boots might be held in charge of the Military Registrar. We hope shortly to have such a stock.

We believe that with a team consisting of surgeon, physiotherapist, chiropodist and cobbler, working on a clinic system of the type outlined, we can avoid the hospitalization of many men and at the same time give efficient treatment. The decentralization of the clinics will save time in travelling and will lift the load from the main orthopædic centres which must continue to treat the cases of major disability.

Finally it appears that we must initiate the scheme ourselves and, when once it is in being, hope that it will receive the support of E.M.S. and military authorities.

Psychological Reactions to Injury

By Louis Minski, M.D., M.R.C.P., D.P.M.

Many members of the medical profession are rarely able to visualize all the needs of the individual whom they are called upon to treat. Probably the commonest example of this failing is seen in the case of the physically disabled. The deformity is in itself so obvious that the surgeon, nurses, and friends may direct all their attention and energies towards its alleviation and the question of mental hygiene is neglected. The result is that morbid psychological factors are introduced because of over-emphasis on the purely physical problem. This is sometimes seen in the case of children who are admitted to

hospital because of some physical injury which is likely to take long to cure, such as fractures as a result of air raids. Because of lack of separate children's wards they are admitted to wards with adult patients, where they are not unnaturally pampered and fussed by patients and staff, and, in fact, spoiled. At the end of some months, when they are fit for discharge, they return to a poor home where they are no longer the centre of attraction, with the result that many of them become difficult and resentful of their surroundings and develop behaviour disorders which are often extremely difficult to eradicate. It will be seen, therefore, that even among children who are not permanently crippled or deformed abnormal psychological reactions may readily occur, while among those permanently disabled "crippled personalities" may be even more easily formed. Many of them show behaviour disorders characterized by aggressiveness, temper tantrums, day-dreaming, stealing, &c., and one of the most important causal factors in symptomatic behaviour in handicapped children is the attitude of the parents towards the child and his disability. Over-protective parents tend to be more protective while an athletic father may show his disappointment in a crippled child by making disparaging remarks to him and increasing the child's feeling of inadequacy. Again, such children often do not enjoy the privileges of other members of the family because "they are too much trouble". The over-protective attitude tends to create "the crippled personality" by making the child more dependent and infantile and totally incapable of living his life as a self-maintaining member of society. Not only parents but teachers, nurses, doctors and all with whom he comes in contact must bear their share of responsibility. The tendency to be sentimental and pity the child may also be associated with a feeling of repulsion for the handicap.

Among children of his own age, however, the crippled child may find greatest unhappiness, as he is often friendless and an object of ridicule. This results in feelings of inferiority and shame with consequent aggressiveness and resentment, or a regression to a more childish level. Over-compensation for these inferiority feelings may often be seen in boasting and attitudes of superiority. All handicapped children, however, are not maladjusted; in fact, many of them show no psychological disturbances at all. Lesions which are acquired early or are congenital are usually well compensated physically, while psychological adjustment is also easier in childhood.

These children have been wisely handled by understanding parents, a tolerant teacher and a well-trained social worker. Something constructive has been offered to compensate for physical handicaps. This may be in the form of adequate recreational facilities and occupational therapy which must be something more than an aid to physiotherapy. It must interest the patient, develop pride in accomplishment and give a feeling of independence. By such means feelings of inferiority and inadequacy, of self-pity and resentment against environment will tend to disappear.

Lesions of the central nervous system such as birth trauma, encephalitis, &c., which produce physical disability often cause at the same time a disturbance of personality which is not a psychological reaction to the physical disablement at all. The personality disturbance and probable intellectual impairment are the direct results of the cerebral lesion which has caused the physical disability. In the same way, in the adult who suffers a cerebral injury or vascular accident, emotional and intellectual disturbances often occur at the same time as the physical symptoms. Patients with partial cerebral lesions may be much more distressed than those with complete ones. In the latter, insight is often lacking and intellectual impairment amounting to dementia may be present. For instance a patient with hemianopia may be very distressed by his disability, whereas a patient with a complete central blindness may be quite unaffected by his loss. Most of these patients, both children and adults, not only require the services of an orthopædic surgeon to attend to the physical deformity but also those of a neuro-psychiatrist.

Among adults there is the group of patients who have lost a limb as a result of an accident which relatives regard as the causal factor in a consequent mental illness. For example, a girl of 25 was said to have fallen under a tube train while trying to enter it and she sustained a laceration of the scalp together with a severed leg. She was an attractive girl, intelligent and artistic, and when convalescent from the physical illness she began to be depressed, said people were staring at her and talking about her. Since that time, viz., two years ago, she has shown signs of an insidiously developing schizophrenia and it is not at all unlikely that the psychotic illness had started before the so-called accident which may have been in the nature of a suicidal attempt. It is wise

not to include this type of case, about which there is some doubt as to the relationship between the physical injury and psychological reaction, but to study those patients who are apparently normal before the accident producing the physical disability and who develop abnormal mental attitudes afterwards. Many such cases of disability and deformity are seen nowadays as a result of war injuries and among the commonest are loss of limbs, blindness and facial disfigurement.

It is not proposed to discuss the psychological disturbances occurring as a result of sepsis, exhaustion, &c., which may take the form of delirious states and toxic confusional reactions, and are not psychological reactions to the physical deformities.

The first adjustment which loss of a limb entails is to that of the phantom limb. This may be regarded as an hallucination occurring in persons with a normal mental setting. Although the limb appears to be very real, the patient has insight into the fact that it is illusory in nature. By subjective perception the limb is perceived as a real one, while by objective perception this impression is corrected mainly as a result of visual impressions. The peripheral theory for the phantom limb assumes that the sensation originates from excitation of nerve ends in the scar and anæsthetization of the stump has abolished the phantom which returns when the anæsthesia has passed away. The cerebral theory maintains that the limb is still represented in the total body image. Head showed that the phantom limb disappeared after injuries of the posterior central convolution and parietal region of the brain. Phantoms are missing in congenital absence of limbs and this is thought to be due to the fact that they have never been represented in the body image. Again, the fact that the arm is much less marked in phantom limbs than the hand may be due to the fact that central representation of the hand is much more extensive than the arm.

Phantom limbs which are not always present may appear immediately after amputation or not for some time. The limb usually feels the same size as the normal one while feelings of irritation and itching and alterations in temperature are not uncommon. For instance, one patient with an amputation through the lower third of the thigh complained of continuous itching below the heel and a feeling as if hot water were being poured down the leg. Pains and cramps in the phantom are not uncommon, the patient often complaining that the toes or fingers are bent in uncomfortable positions. A characteristic of the pain appears to be that it is most marked and persistent where the patient has had a painful wound or scar before amputation. For instance, a patient who had had a wound of the knee with subsequent amputation of the leg felt this painful wound for some time, while another patient whose leg was amputated for senile gangrene was kept awake at nights by a pain in the big toe which had been present before amputation. A woman whose eye had been removed some years before because of severe corneal ulceration which had been extremely painful, developed a painful phantom eye which persisted for some time. On the other hand, those patients who are, like many air-raid casualties, severely shocked at the time they have been injured and have not had to endure for some considerable time the pain of chronic ulceration, gangrene, &c., do not appear to be troubled so much by pain in the phantom limb which, however, is still definitely present. Again, some patients only have phantom limbs when they have pains in them. When an artificial limb is fitted this may be identified with the phantom and may become animated although the latter may be felt to be independent of the position of the body. Adjustment to the phantom limb takes place fairly rapidly, although the pains and cramps in it may give rise to periods of insomnia as they are usually more marked at night. In some cases the insomnia and resulting fatigue tend to produce mild temporary anxiety states.

When the patient is ready for discharge from hospital he now has to adjust himself to his new circumstances. The degree of adjustment which the patient makes depends on a number of factors. The younger the person, as a rule, the better the adjustment, provided that, as previously mentioned, the environment is favourable and the patient is correctly handled. It is found that after the prime of life adaptability is much more difficult although even in younger persons other factors must be taken into consideration. For instance, in the case of a young, attractive, unmarried girl the loss of a leg or facial disfigurement may cause a much more difficult task in adjusting than the loss of an arm, whereas the loss of an arm in the breadwinner of a family who is a manual labourer would be more difficult to adjust than the loss of an eye or severe facial disfigurement. Here again, it is obvious that rehabilitation for the latter in the form of vocational

training for some other form of employment and psychological guidance, and useful creative employment for the former will help to make the mental adjustment more easy.

The previous personality of the patient is also an important factor in the psychological attitude towards an injury. Those who previously showed evidence of neurotic traits are more likely to show abnormal reactions than the stable type of individual. This is well typified in the case of a soldier of 26 who was admitted on 22.6.40 with a compound comminuted fracture of the left tibia and fibula complicated by gas gangrene. The left leg was amputated below the knee. He was quite cheerful while in hospital, made a good recovery, and was fitted for an artificial limb on 16.4.41. He is now at home and doing his previous work of accountancy with the same firm. He is morose, depressed, and apathetic and makes little attempt to interest himself in things generally. It appears that he has always been spoiled by his mother at home, that he is selfish and self-centred and now his mother is very over-sympathetic and over-protective, and she is always giving in to him. This is just the type of environment to produce such a state of despondency in a spoiled and pampered individual who obviously requires a firm but kindly attitude to remove the feelings of dependence and hopelessness.

The comparatively few amputation cases treated at this hospital have made good adjustments and are in employment or doing their housework, apart from one who passed through a severe phase of depression from which he made a good recovery, and the other case already mentioned. None of them show any feelings of resentment, unless sympathetic strangers try to help them, while only one shows any signs of self pity.

It is not only patients with total or partial amputations who are liable to develop abnormal psychological reactions; very often severe or even minor injuries may be opportunities for patients to perpetuate symptoms for some unconscious motive and for which there is no longer any organic basis. This is seen especially in war-time where Service cases who have been wounded continue to have painful scars or stiff joints long after physical factors have ceased to play a part. Very often this is the result of a hysterical prolongation or fixation of symptoms, the motive for the symptoms being that they keep the patient in hospital or at any rate out of active service. These neurotic reactions resemble the compensation neuroses of peace-time in that the symptoms may improve or disappear when the ends are achieved and an adequate pension has been provided. Hysterical exaggeration of symptoms may also occur even when the physical factor is still operative, all these hysterical symptoms arising out of the patient's previous personality; the number of such cases, however, is comparatively few. Psychotherapy in the form of persuasion, suggestion or hypnosis should be started immediately as the longer the symptoms are allowed to develop the more intractable do they become and the more difficult are they to remove.

These symptoms are not consciously produced and the patient does not realize that they are functional in origin. In fact were such symptoms conscious in origin they would express a deliberate intention on the part of the patient to achieve some motive which would help his ends, such a condition being malingering. Often conscious and unconscious motives are combined, and the malingerer may easily persuade himself of the reality of his symptoms.

The following case illustrates the neurotic reaction to a physical injury and at the same time partially reveals the underlying psychopathology. A married woman, aged 34, was admitted to hospital on 24.11.40. She was travelling in a bus with a girl friend during an air raid when a bomb fell near. She felt a severe pain in the left arm and also her friend lying on her, and on looking round she saw the battered blood-stained face of her friend who was dead. She sustained a comminuted fracture of the left ulna and a punctured wound of the neck. The arm was cleaned, the fracture set, and the limb put up in plaster. Union and alignment were good, and when the plaster was removed massage and remedial exercises were ordered. The patient refused to co-operate, became aggressive towards the masseuse and yelled with pain. It was noticed that when attempts were made to move the arm the antagonists contracted at the same time and went into spasm. Manipulation was attempted on 29.3.41 with little result. The arm was abnormally wasted, but no neurological signs were present. She was seen by a psychiatrist as it was considered that a functional element was present. Hysterical contracture was diagnosed and she was given intravenous sodium amytal in an attempt to relieve this and also to make her more receptive of suggestions to aid movements. This was unsuccessful, and

when an attempt was made to straighten the arm she called the doctor a brute, screamed, and wept copiously. As it was considered that there might be some underlying organic cause also, her arm was again manipulated on 29.4.41 when many adhesions in both the shoulder and elbow joints were broken down. She was again given amytal and on this occasion movements of the arm took place. She was given therapeutic talks and left the hospital improved on 11.5.41.

The relevant psychiatric history was as follows: The mother had a withered arm which resulted in her obtaining more sympathy from her husband than she would otherwise have done. The patient had previously had a good personality with no neurotic traits but her husband was a bully and went with other women. He was only kind to her when she was ill and he gave the sister of the ward the impression that he was not anxious to have her home. In addition the patient's children had been evacuated and although she wanted to join them there she was afraid to leave her husband as it would allow him more liberty with other women. There was also the suggestion that the friend who was travelling in the bus with her and who was killed was one of her husband's girl friends. The unconscious motivation for the hysterical illness therefore appeared to arise from (*a*) the fact that her husband was only kind when she was ill, (b) guilt feelings associated with the death of her friend owing to its probably being associated with an unconscious wish for this to occur as a result of her husband's relationship with her, (*c*) the conflict over wishing to join her children and (*d*) the mother having a withered arm which served as an example to her.

This case demonstrates very well the mixture of neurotic and organic symptoms, together with the underlying psychopathology. It should be emphasized that when a physical injury is not making satisfactory progress and physical signs to account for the condition are absent, or when it is definitely suspected that there is a functional component, the services of a psychiatrist should be called upon at once in order that any underlying factors for such a neurotic superstructure may be exposed and dealt with.

It cannot be too firmly stated that a patient may give an impression of having made a good adjustment while in hospital, but after being at home for some time, as in the case of the patient with the amputated leg, psychological difficulties may occur. A wise precaution would be to have all such patients seen by a psychiatrist while in hospital to ensure that there are no personality difficulties, &c., and also to have a social report on the environment to which he is going in order that unsuitable influences can be removed or another more suitable environment found.

I have recently had an opportunity of seeing ex-Service men disabled in the last war. Many of these men have been leading invalid lives for twenty-five years as a result of fractured spines, &c., and the outstanding characteristics of their mental state are resignation and apathy, self-centredness and a tendency to talk about themselves indefinitely. There is however a definite *esprit de corps* and feeling of comradeship, they are willing to help each other and the home whenever they are able, they will do handicrafts if encouraged, but if *ordered* to do anything or strict discipline is enforced they become difficult and obstructive.

Men wounded in this war likely to be permanently disabled are already being sent to such homes and hospitals. This is a great psychological error as these patients quickly realize that in another twenty years they will probably be like the others and they rapidly become depressed, refuse to stay, and are often extremely difficult to manage. Separate homes when the number warrants it should be provided, and until such time arises, beds in other hospitals could be allotted where they would receive psychological encouragement by the admission and discharge of the other patients.

Conditions of the Back Simulating Visceral Disease

By J. H. Kellgren, F.R.C.S.

From the experimental studies on pain carried out by Sir Thomas Lewis and others, we now know that the deep-lying somatic and visceral structures give rise to the same type of pain which is poorly localized and referred over a common segmental pattern. The superficial and peripheral structures give rise to local pain, while from intermediate structures the pain presents every gradation from the full segmental to the purely local type of distribution.

The structures of the back illustrate this general rule very well. The important supraspinous ligament together with the lumbodorsal fascia give rise to local pain. The deep-lying structures surrounding the vertebræ give rise to pain of full segmental distribution, while the intermediate mass of muscle composing the erector spinæ gives rise to pain of

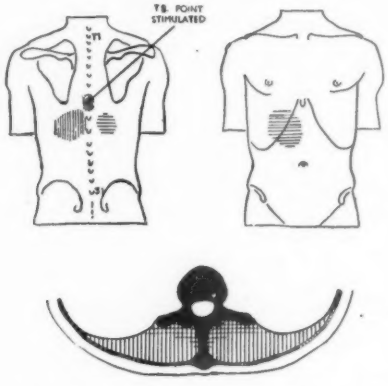


Figure illustrates the distribution of pain arising from structures in the back at the level of the 8th thoracic vertebræ. The supraspinous ligament and lumbodorsal fascia give local pain (dots). The deep-lying structures surrounding the vertebræ give rise to pain of full segmental distribution (horizontal hatching). The intermediate mass of muscle comprising erector spinæ gives pain of modified segmental distribution (vertical hatching).

modified segmental distribution. Besides this variation in pain distribution there is also a variation in the sensitivity of these structures. Thus the supraspinous ligament is intensely sensitive; the structures surrounding the neural arch are somewhat less so, and the vertebral bodies and discs are relatively insensitive. From this it is clear that disease of the insensitive vertebral bodies rarely produces pain unless there is a secondary disturbance of the sensitive neural arch.

Apart from these considerations the clinical picture of spinal disease is determined by the distribution of the segmental pain areas at different levels. Thus from T.11 to L.2, the segmental areas have a very large posterior component, so that backache is the presenting symptom in both spinal and visceral disease at this level.

In the mid-thoracic region the anterior component is by far the greater, so that pain in the chest or abdomen is paramount and such patients are usually investigated for visceral disease to the exclusion of the back; it is this type of patient that provides such diagnostic difficulties.

This is not surprising when we remember that not only is the character and the distribution of the pain identical in both visceral and spinal disease, but pain arising in the back may be associated with the appropriate visceral symptoms and signs; for instance, substernal pain simulating angina may be associated with shortness of breath and palpitations, and the pain may be aggravated by exercise. Similarly abdominal pain may be associated with nausea and even vomiting, and when the appropriate abdominal tenderness and rigidity are added, the clinical picture of visceral disease may be almost exactly reproduced.

Spinal disease might be expected to give rise to pain on movement, but the thoracic spine is easily held rigid during the ordinary movements of the trunk, and such a history is frequently lacking. Pain on movement is also produced by any visceral disease involving the parietes and may therefore be misleading.

It is a safe rule to investigate the back thoroughly as well as the viscera in every patient with pain in the chest or abdomen. The thoracic spine is notoriously difficult to examine, so that I will describe in some detail the method I employ.

First the patient is asked to map out the distribution of his pain, and by comparison

with the segmental pain areas, we can deduce the level of the supposed spinal lesion. The forced movements of the spine are then examined segment by segment, and if the pain is somatic in origin, it will be produced by moving the appropriate segment. Lastly the relevant portion of the back is explored with a needle and novocain when the site of the lesion is further defined and the spinal origin of the symptoms finally demonstrated.

This test of local anæsthesia is not as simple as it sounds. In the first place the pain must be severe at the time of examination for the test to be at all practicable. Secondly it is often difficult to define the exact site of the lesion. The finding of tender spots in the back is frequently misleading as there is always more or less tenderness within the posterior pain areas, and anæsthetizing this referred tenderness leads to nothing but confusion. If, however, we remember that it is only the deep-lying structures surrounding the articular processes and laminæ which give rise to this type of pain, and if we always deduce the level of the lesion from the segmental pain areas, these difficulties are easily overcome.

In this way the spinal origin of much thoracic and abdominal pain can be clearly demonstrated, and it remains only to consider the nature of the lesion. I believe this is usually a simple sprain resulting from some underlying deformity. In the middle-aged the most frequent deformity is a localized kyphosis with retained mobility, but in younger subjects rotation deformities are more frequent. Apart from these sprains every kind of inflammatory or neoplastic disease may be present, but in such cases the diagnosis can usually be established by the X-rays, except perhaps in the early cases of ankylosing spondylitis.

It is important to recognize these cases as they frequently respond to the simple procedure of novocain infiltration followed by hyperextension exercises, and they undoubtedly form the basis of many osteopathic cures to the detriment of our profession. Lastly I would sound a word of warning: these patients are usually middle-aged people in whom visceral disease is common, and although we may relieve their pain by treating their backs, we have in no way excluded the presence of visceral disease.

REFERENCES

KELLGREN, J. H. (1939), *Clin. Sc.*, **4**, 35, (1940), *ibid.*, **4**, 303.
LEWIS, T., and KELLGREN, J. H. (1939), *ibid.*, **4**, 47.

Comment (**C. Jennings Marshall, M.S., M.D.**).—Chronic pain in the trunk without obvious physical signs of organic disease is perhaps the commonest diagnostic problem in the out-patient department—there may be back pain due to visceral disease, there may be anterior pain due to disease in posterior structures, there may be pain both posterior and anterior. For many years I have taught that the questioning of the patient as to the relationship of the pain, relief or aggravation, to visceral functions, and to rest, exercise and locomotion will frequently settle the question whether we have to deal with disease in viscera or in the musculo-skeletal system. There are, however, many cases in which doubt will survive such investigation—visceral symptoms may co-exist with skeletal disease, some visceral diseases may produce pains related positively to rest and motion, and with but few if any visceral symptoms, and the production of referred pain may result in visceral symptoms without organic visceral disease (the numerous forms of abdominal crisis in tabes dorsalis form a useful reminder of such possibilities). The referred pains of such gross conditions as spinal caries, aneurysmal erosion, spinal tumours and metastases offer few difficulties in diagnosis; those of spinal and paraspinal chronic inflammatory lesions of "rheumatic" type are in a rather different category. In the first place the radiographic verification is not so simple as is usually taught; it has been dominated by the idea that osteophytes are pressing on spinal nerves on their emergence from the canal. The osteophytic masses so commonly obvious in X-rays are anterior to the neural foramina and cannot exert pressure on the nerves; even the grossest instances of osteo-arthritis of the spine show little encroachment on the foramina which in addition, compared with the size of the nerve, are very large indeed. (The same knowledge of pathology should be applied to osteo-arthritis as a common excuse for a failure of lumbar puncture!) We very commonly see patients showing great osteophytes in lumbar radiographs in whom questioning gives no history whatever of pain in the appropriate region—the front of the lower limb. The conception of these outgrowths being painful is fundamentally wrong—spinal pains in the vast majority of cases, as

with joint pains in general are not bone pains but ligament pains. (A similar error attributes the pain in cases of avulsion of lateral processes wrongly to the detached piece of bone.) It is of course quite well known that the pain of spondylitis is worst in the early stages when the X-ray signs are minimal or nil. The pains are referred by either, or both, of the classical routes: (1) Direct excitation of the sensory nerve by implication in the inflammatory process (and by infiltration in most cases of carcinomatous metastases), as is seen also in instances of traumatic neuromata, and in implication of nerves in scar tissue; (2) excitation of the central nervous system via the filaments supplying ligaments, &c., and reference out from the segment involved, as in the typical phrenic shoulder pain—the neurologists decline even now to be categorical as to the precise mechanism. When such excitation implicates the region between the 4th and 11th dorsal segments it becomes clear that splanchnic as well as parietal and cutaneous symptoms may arise, simulating visceral disease.

Many referred pains in the trunk arise from conditions farther along the course of the nerves than the neural foramina—the intercostal nerves and particularly the subcostal nerve very commonly are implicated in fibrositic patches, the last-named giving loin-to-groin pain simulating kidney disease and often being associated with a disappointing appendicectomy scar. For over ten years I have taught and practised novocain nerve blocks as both diagnostic and therapeutic measures of the highest value; I published a description in 1936 in *Lancet* (ii), 242.

In dozens of cases the diagnosis has been established clinically in a few minutes by this method in patients who have been submitted to numerous special investigations, often repeated several times—barium meals, cholecystographs, pyelography, barium enemata, test meals, and so on. The value of such tests applied with discrimination is not disputed but the expense, time-wasting and mental deterioration of the patient is far too often overlooked; such repeated examinations, it must be insisted, are one of the most certain ways of rendering permanent a functional disorder.

Diagnostic analgesia is of most certain application where the site of nerve implication is the intercostal space or the lateral parietes; with paraspinal and spinal forms of irritation it becomes distinctly more difficult—all the more as several segments are apt to be involved; where the irritation has permeated the neural foramen it becomes inapplicable in most cases, as it becomes almost impossible to block the affected area to its proximal limits.

Some Spinal Cases of Interest

By E. J. Radley Smith, M.S., F.R.C.S.

These cases have shown either a prolapse of the intervertebral disc or a thickened ligamentum flavum. The former condition is, perhaps, better recognized than the latter, but even the prolapsed disc can closely mimic other spinal conditions as two of these cases will demonstrate.

First are two cases of thickened ligamentum flavum.

(i) A man of 34 fell some 20 ft. off scaffolding thirteen years ago. Ever since he has had pain in the right buttock and leg, sometimes of great severity and increasing in the last two years. His symptoms were strongly suggestive of pain arising by pressure on a nerve root. Pressure on a tender area over the 5th lumbar region caused numbness above the right ankle; standing on the left leg, with the right swinging free, caused tingling all down the right leg. The lumbar curve was found to be flattened; pain was experienced when the sciatic nerve was stretched, and the muscular power of the leg was diminished; sensation on the inner side of the ankle was diminished (4th lumbar); the ankle-jerk was unaffected. The cerebrospinal fluid revealed no abnormality.

The history and signs suggested to us a prolapse of the intervertebral disc on the right side, probably between the 4th and 5th lumbar vertebræ. Lipiodol injection was made, using only 2 c.c., and the column studied as the patient was tilted under the screen. The antero-posterior films showed a constant narrowing between 4th and 5th lumbar vertebræ (fig. 1). Lateral films were taken in the prone position, and these showed that the indentation in the lipiodol was chiefly at the back (fig. 2). In this way, the diagnosis of thickened ligamentum flavum was made before operation.

Laminectomy was performed, and the ligamentum flavum between the 4th and 5th lumbar vertebræ found to be about three times its usual thickness and also notably white

instead of yellow. The dura was much compressed, but expanded normally when the ligament was removed. No prolapse of the disc was seen or felt. The patient was up in one month, and practising golf shots in two.

(ii) The second case is, in many respects, similar. The patient is a schoolmaster, aged 42, who first began to suffer low lumbar pain five years ago, after he had been chilled while gardening. The pain was entirely lumbar for some ten days and then suddenly radiated to the left leg. For the next four years he suffered from intermittent "sciatica" and numbness of the foot, of such severity that he submitted himself to most forms of physical treatment, manipulative stretching of the sciatic nerve and epidural injection.

When admitted in 1940 he had severe left-sided sciatic pain. The usual signs were all present: wasting of calf and thigh; absent ankle-jerk; diminished sensation on the outer side of the ankle; and pain on stretching the sciatic nerve. The cerebrospinal

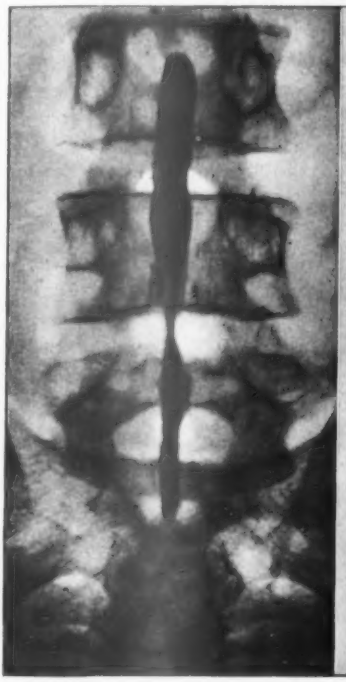


FIG. 1.

FIG. 2.

fluid showed no abnormality. The lipiodol studies showed a narrowing opposite the disc between the 4th and 5th lumbar vertebræ, but unfortunately attention was not directed, during screening, to the possibility that this narrowing might be postero-lateral, rather than antero-lateral. Changes similar to those described in the preceding case were found at operation. This man has now remained well for some eighteen months.

At the moment it does not seem possible to differentiate clinically, with any degree of certainty, between the prolapsed disc and the thickened ligamentum flavum. Although the so-called "hypertrophy" of this ligamentum flavum was described by Elsberg as long ago as 1913, little attention seems to have been paid to it in this country until recent years. Careful screening, or radiography, in the lateral plane, after lipiodol injection, appears to be the only method of separating these two groups. The lateral films are unhappily not so easy to take with advantage, since the lumbar curve causes the lipiodol

column to run off the hill in the supine position, or into the valley in the prone. However, since the surgical approach is the same, the differentiation may not have much practical significance.

The prolapsed intervertebral disc in the commonest situation—the lower lumbar spine—produces sciatic pain with, usually, low backache. If the prolapse occurs in other regions of the spine, a quite different picture is produced.

(iii) The next case is of a prolapsed disc in the common site. He was a stoker, aged 29, who had suffered no single severe back injury, but had "sprained" the back slightly many times while shovelling coal with the back bent. The typical history of low backache, for three months, followed by left sciatic pain and pins and needles on the outer side of the left foot, both for nine months, was given. He showed the usual signs of flattening of the lumbar spine; absence of ankle-jerk; pain on stretching the sciatic nerve and on pressure on the tender 5th lumbar spinous process; slight wasting of the calf and blunting of sensation over the outer side of the foot, ankle and calf. The cerebrospinal fluid was normal. The lipiodol films showed an enormous indentation of the column on the left side, opposite the disc between the 5th lumbar and 1st sacral vertebræ. Laminectomy confirmed the existence of a large prolapse of the disc in this situation.

(iv) The next case, diagnosed by Professor Nevin as one of spinal tumour, was a lorry driver, aged 37, who had had no injury but who started his heavy lorry by "swinging" it. For four months before admission, both legs had felt cold and heavy; walking was becoming increasingly difficult. He showed a spastic paraplegia, with a skin level pointing to a lesion in the region of the 7th or 8th thoracic spinal segment.

The cerebrospinal fluid findings are illuminating. On 3.3.41 the lumbar fluid contained 1 cell and 80 mg. of protein, with very little rise in the fluid pressure on jugular compression. On that date, 2 c.c. of lipiodol were put in by the lumbar route. Films taken with the patient sloping, head downwards, were not satisfactory. Therefore on 6.3.41 1 c.c. of lipiodol was injected by cistern puncture, so that the upper level of any spinal block could be seen. The fluid drawn off from the cistern—3 days after lipiodol had been injected into the lumbar subarachnoid space—contained 35 cells! This film of the cistern lipiodol revealed a block opposite the space between the 5th and 6th thoracic vertebræ, and the outline was said to suggest an intramedullary spinal lesion. On the day following cistern puncture, retention of urine developed, and laminectomy was performed at once. The ligamentum flavum was found to be normal in thickness and yellow in colour. The dura and cord were displaced considerably backwards by a tumour in front of the canal, and a prolapse of the disc between the 5th and 6th thoracic vertebræ was found on the left side. No other spinal tumour was found. Another, but rather smaller, prolapse was found on the right side of the same disc. For a few days after operation paralysis of the legs, incontinence and abdominal distension—doubtless due to operative trauma—caused some anxiety, but he made an excellent convalescence, and left hospital fully recovered four months after operation.

This case reminded us that a prolapsed disc, above the termination of the cord instead of in the region of the cauda equina, is usually diagnosed as a spinal tumour. I believe a bilateral prolapse of one disc is decidedly rare. Also we were afforded the opportunity of observing the fluid a few days after the injection of lipiodol and found 35 cells present!

(v) The last case is of a cervical prolapsed disc which was also diagnosed, not without justification, as a spinal tumour, and which, again, caused bilateral nervous signs with an almost complete spinal block.

Comment (**Harvey Jackson, F.R.C.S.**).—The clinical picture induced by herniation of the nucleus pulposus varies in accordance with the spinal level at which the protrusion occurs. Whereas in the lumbar and lumbosacral regions the diagnosis depends on differentiation from the many possible causes of sciatic pain, at other levels in the spinal axis the clinical appearances are those of spinal compression.

The incidence of nuclear prolapse in a total series of patients claiming relief for pain of sciatic distribution is limited to a small percentage. At the neuro-surgical centre of which I have charge, of all the patients admitted with the provisional diagnosis of "sciatica, probable hernia of the disc", only about one in every ten is finally subjected to operation.

The isolation of the patient harbouring a prolapsed disc is no simple clinical problem; rather does it depend on careful clinical selection amplified by apposite investigation. At the present time I am not aware of any specific clinical syndrome of truly pathognomonic import, yet it may be said that a clinical impression can be formulated. In an analysis

of relative clinical phenomena, both historical and physical, numerous factors assume significance, though none is conclusive. A history of injury may or may not be elicited, nor indeed need injury be sustained. Lumbar pain is the heralding symptom, to be succeeded after an interval of weeks, or perhaps months, by extension of the pain along the course of the sciatic nerve, over part or the whole of its distribution. The pain runs a periodic course with intervening spells of complete relief. Exacerbation of the pain on coughing, sneezing, or straining may be described, as with any root pain, but this, *per se*, may be equally marked in conditions of chronic back-strain; moreover it offers no aid in the separation of neuritic from pressure types of sciatica. A fair proportion of patients find that the pain is apt to increase on the adoption of a sitting or recumbent posture; hence the statement may be volunteered that getting out of bed and walking about is the only means of relief. Changes in the lumbar spine are essential components of the clinical picture; thus one finds obliteration of the lumbar concavity, scoliosis, and restricted mobility, the degree of each varying from case to case. Spasm of the erector spinæ is usually present, with the result that it stands out boldly, more on one side than the other on account of the scoliosis. Neuritic signs (Laségue, tenderness over the sciatic nerve, diminution of power at the ankle, wasting, diminution or loss of the ankle-jerk, disorder of sensation over relative root zones) may or may not be present, though such findings will afford indication of the actual spinal level involved. Exacerbation of pain on jugular compression would appear to be inconstant and inconclusive.

Plain radiographic examination is said sometimes to reveal diminution of the affected intervertebral space; so far I have failed to observe this.

Lumbar puncture, with manometric determinations of cerebrospinal fluid pressure and estimation of the total protein content of the fluid, may produce valuable information. An absolute spinal block would be obvious, but such a disclosure is unusual with disc prolapse, rather indicating the likelihood of an underlying tumour; certainly such evidence would exclude neuritis. The employment of Queckenstedt and inverse Queckenstedt tests appears inconclusive. As for protein content, in the absence of a complete block, the percentage elevation bears no relation of consequence to either prolapsed disc or neuritis, though a normal content favours prolapsed disc rather than neuritis.

Foci of infection having been eradicated, there remains observation on the reaction of the patient to simple remedial measures, e.g. radiant heat and massage, diathermy, epidural or perineural injections of saline or novocain, or, in suitable cases, spinal manipulation together with stretching of the sciatic nerve. Some cases indicate resort to more drastic measures from the onset, but never have operative means been undertaken unless conservative methods have been applied and failed to produce lasting relief.

At this stage it is felt that the adoption of surgical treatment must be seriously considered. First of all, however, it is demanded that the patient is incapacitated from full normal activities by his affliction. Before resort to surgery is undertaken confirmatory evidence is sought by employing contrast radiography, utilizing air as the contrast medium. Air myelography is no certain procedure, for satisfactory radiographs cannot be produced in patients of heavy build; nevertheless it merits employment. The use of lipiodol, or other similar preparation, is avoided until immediately before exploration, and it is utilized then only for purposes of study, in the hope that finally a form of investigation may be evolved to the exclusion of such methods. I should like to appeal for the relinquishing of the generalized use of lipiodol as a diagnostic medium, because unpleasant reactions are apt to follow its injection, such reactions varying between increase of the original pain and the initiation of a diffuse meningeal irritation. The removal of lipiodol through a wide-bore needle has been effected by several observers, but only after prolonged manipulations not devoid of risk. That this can be done does not, in my opinion, justify its indiscriminate application.

The operative appearances vary. A hypertrophic state of the ligamentum subflavum is encountered frequently in the operative exposure. When other causes fail to be revealed, the pain is ascribed to this thickened ligament. I am not convinced that this is an adequate explanation. Rather do I believe that it is consequent on the scoliosis and is therefore the result of the lesion and not the pathological basis of the pain.

Herniated discs in the lumbar region produce two special forms of protrusion. One form is a spheroidal, or knob-like protrusion found to one side, and encroaching on the spinal canal by the side of the posterior common ligament of the spine. The other type consists of a mound-like elevation situated in the middle line and clothed by the stretched posterior common ligament and the dura mater. Those found in the dorsal spine present yet another form, for a lesion mimicking a chronic tuberculous abscess

occurs. This protrusion contains a substance of the consistency of caseous matter; moreover the periphery is apt to consist of a calcified capsule. Such calcification may, in fact, cast a shadow of such density on the radiograph as to allow of recognition on straight films.

Some Points in the Diagnosis of Osteochondritis of the Knee

By C. D. Langton, F.R.C.S.

A small series of 13 cases of osteochondritis dissecans of the knee was treated at Horton Emergency Hospital, Epsom, in the fourteen months, April 1940 to May 1941. During this period a total of 276 cases of knee disorders were admitted, traumatic, infective, degenerative and neoplastic. Thus osteochrondritis constituted 4·7% of the total. This large proportion is probably accounted for by the fact that the greater part of our knee cases are military, and that trauma is, by far, the most common cause of their disability. It must also be stated that 6 of the 13 cases had a torn intra-articular cartilage as well as the condition under review, and in 3 of these the osteochondritis was unsuspected, as it did not show in the X-ray.

All but one case gave a history of trauma, though two were a little vague—one stating that he had played a good deal of football and had hurt both knees many times, though never seriously, while the other's peace-time occupation involved considerable kneeling. The type of injury was nearly always a twist—in one case the man fell 12 feet through a skylight on to his flexed knees. Nearly all the histories, however, tended to conform to a definite pattern. Following an injury to the knee, there was pain and effusion, which soon subsided, though the joint did not become quite normal—some pain on movement, aching at rest, recurrent small effusion, or instability of the joint—any or all of these symptoms persisting for a time varying from nine years to four months, with an average of three years, until suddenly, either spontaneously or following a second injury, all the symptoms were aggravated, with, in some instances, the addition of locking. In only one case could this latter be attributed to the liberation of a loose body into the joint; while in three, it was unassociated with either a medial meniscus injury or the presence of a loose body. The locking can be explained by the fragment becoming more mobile, though still attached to the femoral condyle, the new mobility allowing it to get caught between the femur and the intact medial meniscus. Admittedly, lateral meniscus injury is not entirely excluded as the cause of the locking, though in every case it was examined, as well as possible, from the incision on the internal side of the joint, and apparently was intact. However, with such a small total number of cases, it may well be that 3 out of 13 had a damaged external meniscus, without physical signs indicating it, though no knee locked after operation in spite of ample opportunity during the subsequent rehabilitation and physical training. Unfortunately all the histories did not conform to this cut-and-dried pattern, but it does seem that there is something diagnostically helpful in the sequence outlined above.

On examination of the joint, little reliable evidence of the presence of the condition was detected. The only constant sign was wasting of the quadriceps. Limitation of movement and crepitus occurred in some cases. Tenderness on deep pressure over the affected area was present in the majority, but as this included all 6 cases with torn internal meniscus. it is impossible to say how frequently it is present in uncomplicated cases.

In the literature on this subject, X-ray examination has usually been accepted as settling the diagnosis, and so, of course, it does when positive. In 5 of our 13 cases, however, the X-ray was negative. The obvious reason for this is that the loose fragment contained only cartilage, but this was found to be incorrect. I have suggested two other reasons besides the absence of bone for a negative X-ray:

(1) The actual fracture line is too thin to show on the film. An exact parallel can be seen in fracture of the carpal scaphoid. Lachmann (1938) showed experimentally that a gap of at least 1 mm. between the opposite bony surfaces is necessary before the line of separation in the knee is visible. He excised a piece of bone and cartilage from the internal femoral condyle of a cadaver, replaced it, and took antero-posterior and lateral X-rays, gradually increasing the separation of the fragment by coating its bony surface with a measured thickness of a radio-translucent medium. The line of separation showed first in the lateral view when there was 1 mm. of separation, and in the antero-posterior with slightly more.

(2) To show, with even 1 mm. or more of separation, providing there is not *gross* dis-

placement, the rays from the tube which will show the lesion on the film must be tangential to the femoral condyle at the point of the lesion. This is commonly so with the central ray when the knee is X-rayed in the conventional positions, but if the lesion happens to be a little higher on, or more to one side of the condyle than usual, it may not show in the X-ray, unless special positions are taken.

Accordingly I submit that a normal pair of X-ray photographs will not rule out a diagnosis of osteochrondritis; careful examination is necessary, many films requiring to be taken with a tube shift accurately measured, before there is even a reasonable probability that there are no bony changes.

Perhaps here is a reason for some of the lack of knowledge as to the origin of loose bodies in joints; further, as we know that flakes of cartilage in a knee can be absorbed, is it stretching the imagination too far to postulate that eventual arthritis can originate in this way, and that, with more accurate diagnosis and earlier operation, we may be able to diminish its incidence from this cause?

How long does it take after the causal injury for evidence to show on X-ray? That is, how long does the sodden, fibrous tissue or fibro-cartilage, found in the base of the crater in the femoral condyle, take to attain a thickness of 1 mm. Our figures do not lead to any definite conclusion, though in one case the separation is visible, in the lateral view only, in six months.

As final points in the X-ray appearances of this condition, I would mention that the general description of a small, dense area of the medial femoral condyle, surrounded by a translucent zone, is not always correct. As is well known, the bone in the partially separated piece may be alive—nourished through a tag of the posterior cruciate ligament—and it will not necessarily appear denser than the normal condyle. In fact it sometimes seems more translucent, even though completely necrosed, the explanation being that with the X-rays tangential at the site of the lesion, they have so much less depth of bone to traverse than the rays passing through the much thicker normal condyle.

It is not intended to discuss the treatment of osteochondritis, though the bearing which an earlier diagnosis would have on this may be mentioned. The onset of arthritis has already been referred to, and it is only reasonable to suppose that early operation would lessen its incidence, though a number of knees may be opened unnecessarily. Further, Axhausen (1914), Kappis (1920) and Moreau (1923) have recorded cases of spontaneous cure. What should be done for a patient giving a history on the lines sketched earlier, who has tenderness over the condyle and a wasted quadriceps, but a normal X-ray, is a subject for further work, which should not be on the "look and see" principle. Few of my points are precise, and this should serve to restrain those of very radical tendencies.

A last personal opinion is that the transverse incision along the joint line from the medial collateral ligament to the ligamentum patellæ, is inadvisable for removal of the medial meniscus, as 6 operations—out of a total of 49—for removal of a torn medial meniscus were found to be complicated by osteochondritis. The condyle can be inspected well enough through this incision, though at the expense of extending the knee during operation, but it is impossible satisfactorily to remove a partly attached fragment and to bevel the edges of the resulting crater.

To summarize, a series so small as 13 proves nothing but the need for more accurate diagnosis. Many more cases are necessary before definite conclusions can be reached about the points which suggest themselves. However, as far as they go, it seems that a history conforming to type, tenderness over the point on the condyle likely to be affected, crepitus, especially if restricted to a small arc in the total range of movement, and a wasted quadriceps—if all present together—should make one suspect the presence of osteochondritis in the absence of X-ray changes. Finally, some research in the realms of radiology is definitely indicated.

REFERENCES

AXHAUSEN (1914), *Arch. f. klin. Chir.*, **104**, 581.
BALENSWEIG (1925), *J. Bone & Joint Surg.*, **7**, 465.
BURR (1930), *Canad. M. A. J.*, **41**, 232.
CONWAY (1934), *Ann. Surg.*, **99**, 410.
Id. (1937), *Am. J. Surg.*, **38**, 691.
FAIRBANK (1933), *Brit. J. Surg.*, **21**, 67.
KAPPIS (1920), *Deutsche Ztschr. f. Chir.*, **157**, 214.
LACHMANN (1938), *Radiology*, **31**, 521.
MOREAU (1923), *Arch. franco-belges de Chir.*, **26**, 131.
PHEMISTER (1924), *J. Bone & Joint Surg.*, **6**, 278.

Lumbar Puncture Injuries

By A. D. Everett, M.S., F.R.C.S.

Injury to an intervertebral disc is still rarely thought of as a complication of lumbar puncture. In the three cases on which this paper is based, the condition was discovered while investigating the cause of persistent low back pain following this procedure.

Billington (1924) reported twelve cases of a similar nature which he described as spondylitis following cerebrospinal meningitis. Pease (1935) wrote an authoritative article based on three cases. Milward and Grout (1936) recorded five cases following spinal anæsthesia, and one further case was described by Gellman (1940). In all these cases the main signs and symptoms were essentially the same as in the present series.

Clinical features.—In each of the cases described the patient complained of persistent low back pain coming on a few days after the lumbar puncture. This pain was made considerably worse by exercise, and especially by any flexion of the spine. A certain degree of stiffness after sitting for any length of time was also experienced. On examination, a marked degree of rigidity of the lumbar spine was present, with a flattening of the normal lumbar lordosis. In one case there was actual angulation backwards, with the apex at the 4th lumbar spine. Radiographs showed collapse of the intervertebral disc relating to the space used for lumbar puncture. This was evidenced by gross narrowing of the space between the vertebral bodies. Individual features were also present in each of the three cases. In one there was clinical and radiographic evidence of infection of the bodies of the vertebræ above and below the disc involved; this was sufficiently marked for the radiologist to query tuberculous infection of the spine. In a second case osteophytic outgrowths on the anterior surface of the bodies of adjacent vertebræ were a conspicuous feature, while in a third the radiographic evidence of collapse was not present for the first two months.

Treatment and results.—One patient was treated on a plaster bed in extension for three months, and then for a further three months by graduated exercises and physiotherapy. He made an exceedingly good recovery, and was boarded back to the Army category "C," with a recommendation that he should be upgraded in a further three months. The second patient refused all treatment except fourteen days' rest in bed. This patient undoubtedly showed the least improvement, and when seen three months after discharge had still not returned to work and was complaining bitterly of his back. Radiographs showed complete collapse of the disc, and marked osteophytic changes round the vertebral bodies involved. The third case remained untreated except by physiotherapy for six months. This was because when he was first admitted to hospital there was no radiographic evidence of collapse. It was not until he was readmitted to hospital some six months later that the condition was discovered. He was then treated by a lumbosacral belt which made him very much more comfortable. The two main sequelæ that are still present in all three cases are difficulty in lifting weights from the stooping position and stiffness of the back after sitting for any length of time.

I agree with Pease that the probable causation of the condition is a slow seepage of the nucleus pulposus through the annulus fibrosus. Whether this occurs directly through a tear caused by the lumbar puncture needle, or whether the needle sets up an inflammation in this structure which weakens it, as suggested by Milward and Grout, it seems impossible to say, but in none of our cases was there any evidence of prolapse of the nucleus pulposus, which is the condition one would have expected if the annulus fibrosus had become weakened by an inflammatory reaction. In some cases it seems certain that there is also present a mild low-grade infection which causes an osteomyelitis of the spine. Whatever is the actual mechanism, the changes in the bodies are obviously secondary to the disc changes.

CASE NOTES

(1) A soldier, aged 21. On 15.2.41 a diagnostic lumbar puncture was done, with some difficulty. A few days after this he began to complain of low back pain. This apparently got steadily worse during the next few weeks, being especially bad towards the end of the day, when he could hardly walk. Great pain on stooping and sitting down.

On examination (end of March).—Temperature 99·4°, rigidity of lumbar spine with angulation, the spine of the 4th lumbar being prominent. X-rays showed elimination of intervertebral space between 3rd and 4th lumbar, with considerable erosion of adjacent

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 1 (*Case 1*).—Taken within a few weeks of lumbar puncture, showing considerable collapse of intervertebral disc and erosion of the bodies of the vertebræ above and below.

FIG. 2. (*Case 1*).—Towards the end of three months on a plaster bed. Note eroded area considerably less in extent and slight forward displacement of L.4.

FIG. 3 (*Case 1*).—Taken four and a half months after beginning treatment. Patient now on remedial exercises. Note considerable diminution of joint space and slight sclerosis of vertebral bodies which are otherwise returning to normal.

aspects of the bodies of these vertebræ (*see* fig. 1). A blood sedimentation rate was done and showed a mean of 13 mm. for the two hours. A diagnosis of low-grade infection of the spine, ? cause, was made and the patient put in a plaster bed.

During the next three months patient became symptom-free. His pyrexia subsided in the first few days and his blood sedimentation rate came down to a mean of 5 mm. X-rays taken during this time showed a steady improvement of the eroded area (*see* fig. 2).

At end of June patient was allowed back into an ordinary bed, and at the end of July started to walk.

X-rays taken in August showed no sign of bony disease, but still evidence of disc collapse (*see* fig. 3). Patient was put on remedial exercises, and by the middle of September was doing full physical training. He still had some limitation of flexion and complained of difficulty in lifting weights from the stooping position. Apart from this he was symptom-free.

At end of September patient boarded back to the Army Category "C", with a recommendation for up-grading in a further three months.

(2) Sailor, aged 25. In October 1940 patient had two diagnostic lumbar punctures in one week. When first seen in November, six weeks after lumbar puncture, he was complaining of low back pain made worse by exercise.

On examination.—The lumbar spine was rigid, but there was no tenderness. X-rays showed a spina bifida, but otherwise nothing abnormal. A diagnosis of fibrositis was made, and physiotherapy given. In February 1941 lumbo-sacral belt fitted, pain in back less. In April 1941 pain improved but still pain on semiflexion and now some tenderness over 4th and 5th lumbar. X-rays showed narrowing of joint-space between 4th and 5th lumbar.

June 1941 patient discharged wearing his belt and fairly comfortable.

(*See* account of case by P. G. Epps, Sect. Orthop., p. 220, this issue).

FIG. 4 (*Case 3*).—Showing diminution of intervertebral joint space due to collapse of disc.

(3) Builder, aged 29. On 14.3.41 spinal anæsthesia for hernia operation. This presented some difficulty. The patient was discharged on 13.4.41, but returned as an out-patient on 21.5.41 complaining of aching pain in lower part of back and right buttock. This pain was made much worse by any flexion of the spine such as sitting down or lifting weights from the stooping position.

On examination.—Tenderness over 3rd and 4th lumbar spines and all movement of spine in this area limited. X-rays showed gross diminution of intervertebral space between border of the 3rd and 4th lumbar vertebræ (*see* fig. 4). The patient would not agree to a plaster bed or spinal jacket. He was kept fourteen days in bed after which he refused further treatment. He was kept in hospital for a further few weeks with modified rest. At the end of July X-rays showed no appreciable change and the patient was discharged.

In September he was seen again as an out-patient and was then complaining bitterly of his back. Could not lift weights and could not sit for any length of time. X-rays showed complete collapse of disc with considerable osteophytic outgrowths on anterior surface of bodies.

REFERENCES

BILLINGTON, R. W. (1924), *J. A. M. A.*, **83**, 683.
GELLMAN, M. (1940), *J. Bone & Joint Surg.*, **22**, 980.
MILWARD, F. J., and GROUT, J. L. A. (1936), *Lancet* (ii), 183.
PEASE, C. N. (1935), *Am. J. Dis. Child.*, **49**, 849.

Section of Orthopædics

President—C. LAMBRINUDI, F.R.C.S.

[*November* 22, 1941]

PRESIDENT'S ADDRESS

The Role of Orthopædics in Medical Education

By C. LAMBRINUDI, F.R.C.S.

IT is tempting and certainly easier to choose as a subject for an Address, one of the many problems connected with war surgery, but, when everything is in the melting pot, all old habits subjected to scrutiny, "Planning" rather than "Wait and See" the trend of the day, I would like to use this privileged occasion to examine our system of medical education, with particular reference to the role that orthopædics is, I hope, destined to play in it in the future.

During the last war, it required all the persuasive genius of Sir Robert Jones, before orthopædic surgeons were given a fair trial; in this one there are not enough to go round.

After the last war, one teaching hospital after another appointed an orthopædic surgeon to its Staff, now most of them have two. Chairs of orthopædic surgery have been created in several universities.

In thinking about orthopædics and education, one must, of course, draw a distinction between the education of an orthopædic surgeon, and the place that orthopædics ought to take in the general training.

The question we ought to ask ourselves is, not how much orthopædics should a student be taught, but rather how may orthopædics be used to enhance the intellectual equipment of the budding general practitioner. Put in that form, emphasis is laid, as it should be, on education, and not specialization.

The medical educationalists of to-day are the general surgeons and physicians. It is they, in the main, who arrange the curriculum, and see to it that the student does not enter the mysteries of the special departments until very late in his career, when he is almost rushed through them.

Our medical and surgical colleagues have a profound distrust of specialists, and whenever a part of general medicine or surgery is nipped off and takes the form of a specialty, it is cast aside and put into the background so far as teaching is concerned, always on the plea that a student must have a general training before he can specialize.

This habit has become cemented by tradition. Priestley puts it aptly, when he says that: "Tradition is meant to be a Guide and not a Jailer." In the pre-clinical period the teachers and examiners are all specialists, in the clinical period the teachers and examiners are in the main general surgeons and physicians. Which is the right tradition? It is pertinent to ask: Are we becoming jail-birds?

In the pre-clinical period, the specialists are physicists, chemists, biologists, anatomists and the physiologists. They all work together for the benefit of the student, and as far as I know, not one of them abrogates to himself a special place of authority. The final product of that period is good, especially lately since anatomy is being taught with more imagination. When we first meet the student, after he has passed his Second M.B., he seems on the whole to be well trained, facts have been presented to him in an orderly manner, he does not appear too muddled and is ready for the next step forward in his career.

But when he enters the wards, that method of teaching through a series of graduated and well-balanced specialties, which worked well in the past, is abandoned. He is plunged into a new world, a new emotional state, has innumerable strange names, and a huge variety of strange pathological conditions flung at him, none of which appear to him to be connected one with the other, and still less with the mechanics, biology, anatomy and physiology which he has already learnt and been taught to believe were the foundations of his future activities.

His foundations, acquired with such labour, are suddenly taken from him, and a strange

thing called pathology is prematurely put in their place. He is thrown into utter confusion.

We, who work in a department where the student population consists of final year men about to take their qualifying examination, see this confusion. We find that their powers of observation and deduction are disappointing, and that they have forgotten their anatomy and physiology; consequently when the more enterprising of them attempt to apply what they have learnt in the general wards, to what they see in our department, it almost invariably is in terms of pathology. More often, however, they make very little effort to apply their knowledge, and even fail to detect signs of inflammation. In other words, even at this late stage, when they enter a new sphere, they apparently cut themselves off from a lot that has gone before, and start afresh.

The fact is, that all students are " specialists ", with that type of single-track mind which the general surgeons and physicians abominate so much, and try, so hard and unsuccessfully, to crush. This is a fact that we teachers must accept, and not fight against, for it is a normal process of intellectual development.

Whenever a crisis arises through poor examination results, the remedy is always the same, more or different registrars, and more classes. I have never heard the subject of medical education broadmindedly discussed in Committee, or a doubt raised as to whether we were presenting the material to our students in a palatable and coherent form.

This tendency to " specialize ", in its narrow sense, or, if you like, learning in a series of more or less watertight compartments, is a characteristic of the growing mind. A child " specializes " in crawling before standing, in standing before walking, in a tricycle before a bicycle, and so on all along the road to maturity. That as he grows he can " specialize " in an ever-increasing number of things, does not alter the fact, that his approach to each in turn is that of a single-minded " specialist ". Multiplicity of " specialisms " does not of itself make for breadth of vision or wisdom, only the process of integration, which is the very essence of maturity, can do that.

Maturity may appear precociously, more often in the late twenties, too frequently never at all, and there are many in high places, wielding authority, whose intellectual development has not progressed beyond the " multi-specialist " stage. There is one thing certain, and that is that passing the Second M.B., or attaining a certain age is not the yardstick by which to measure it, or the signal to abandon a method of teaching suitable to immature minds. I doubt if anything can hasten maturity; confusion can most certainly delay it, perhaps even frustrate it, and I am convinced that, what must be to the student a jumble of " multi-specialties " presented in haphazard sequence, which goes by the treasured name of general training, is not the best introduction to clinical medicine.

Pari passu with this mania to " specialize ", the developing mind shows a strong inclination for the association of ideas. Provided the association is obvious, it will seek to explain a new phenomenon, which it does not quite understand, in the light of what it already knows. A child, for instance, when he first sees an aeroplane, will call it a bird. It is a kind of mental reflex, one which all wise teachers of the young appreciate and make use of, and must not be confused with the purely intellectual process of selecting material for comparison.

Our medical educationalists should not try to crush normal peculiarites of intellectual development. Instead, they should utilize them and so arrange the curriculum that subjects follow one another in logical sequence, choosing for the first, those which have an obvious bearing on mechanics, anatomy and physiology.

In this connexion I have had an illuminating experience. On account of the scattering of our school, my dressers now consist of final year men as before, and first year men fresh from the Second M.B. One day, at the beginning of the war, a patient appeared at Out-patients with a paralytic equinovarus, walking with a marked limp due to paralysis of the glutei muscles. I asked the students if they thought the limp would be improved if I corrected the deformity of the foot. The senior men said " Yes ", and talked learnedly about a subastragaloid arthrodesis, the junior men said " No, because he is walking with a tilted pelvis ". In all my experience of teaching senior students, I have never had that answer given me so spontaneously. These raw young men had spotted for themselves the Trendelenburg limp, and there was no difficulty whatever in explaining to them its diagnostic significance.

Naturally, my first impression was that they were exceptionally intelligent. But, on further reflection, I realized that they were merely displaying normal reactions. Faced

with a problem that had an obvious bearing on the only medical knowledge at their disposal, anatomy and physiology, they automatically applied it and gave the correct answer. In the manner of any healthy young animal when placed in its proper environment, they were educating themselves and opening up their association tracts. It is not so much that the senior men had forgotten the broad facts of anatomy and physiology, but they had never been placed in the suitable atmosphere at the right time in which to learn how to apply it. These association tracts had never been used. Yet, they too, responded to my question in a perfectly normal manner.

The difference between them was their mental reflexes, or training, not their knowledge or intelligence. For two years the young men had been trained to think in terms of anatomy, physiology and function, whilst for the last three years, the older men had concentrated on disease, deformity, and operations, the fundamental subjects lay dormant, unassociated, isolated. I do not think that I am guilty of over-emphasis, if I repeat that according to their respective lights, both these sets of students reacted to the stimulus of my question in a normal way. But, it is a reflection on a system to regard it as normal that junior men should recognize and interpret a case requiring a knowledge of fundamental subjects, more readily than their older and more erudite companions.

I do not want to imply that it is a calamity to fail to spot the details of a case of infantile paralysis, but it does seem that orthopædics offers an excellent opportunity to put into practice the knowledge gained in the pre-clinical period without introducing too much that is new and confusing. Indeed, in my experience, the junior men take to orthopædics and seem to profit from what it has to teach very much more than senior ones. What is needed, is, so to speak, a grammar of Clinical Medicine, something that will take the place of Latin and Greek in a general education, which aims not so much at instruction, but in training the mind. I believe, that we, together with some of our other specialist colleagues, could write it.

The subjects I would choose would be orthopædics including fractures, neurology including elementary psychology, and urology. All these are essentially anatomy and physiology, they are all to some extent connected one with the other, and they are neither wholly surgical nor wholly medical, but a combination of the two.

What better exercise in applied anatomy and physiology, than localizing a neurological lesion, or a bleeding point in the genito-urinary tract?

I would include urology, because of its precision, its nice use of instrumentation, and the comparatively simple nature of its physiological and biochemical tests; moreover, the mechanical effects on the viscera, due to obstruction, are beautifully and simply demonstrated by X-ray and, the secondary effects on the cardiovascular system are well within the competence of a student fresh from his Second M.B. to understand. In fact, in that compact subject he will see in miniature and in easily demonstrable form all the mechanical and physiological principles of visceral surgery.

Orthopædics too, with its emphasis on function rather than extirpation of disease, has a special educational value in the early clinical period. It is almost entirely applied mechanics, anatomy and physiology, with just enough pathology to be a stepping stone to profounder studies later. It gives an excellent training in observation and deduction, for apart from X-rays, it requires no aids to diagnosis, only the eyes, the fingers, and an accurate taking and evaluation of history are needed. Moreover, fractures offer a good opportunity for the first intimate contact between student and patient.

What better exercise in observation, than interpreting a limp, or in applied anatomy, than analysing a case of infantile paralysis, and planning a tendon transplantation or some other operation to improve function? I am not going to labour the value of fractures, their production, reduction, and treatment by adequate splintage as a lesson in applied mechanics, but a word or two about posture is not out of place. It shows a lack of sense of proportion, that a student should have to wait to the end of his training before the true significance of that huge group of minor ailments, attendant upon poor body mechanics, is revealed to him. The symptoms to which they give rise, local pains, referred pains, referred tenderness, low level of health, often so simulate organic disease, that they will frequently have seen such cases in the general ward subjected to routine examinations, even laparotomy, with negative results, before the true nature of the symptoms were appreciated. Posture, and maluse of the whole or part of the body, is a physiological problem. It is connected with muscle tone, reciprocal innervation of muscles, their grouping into agonists, antagonists and synergists, and requires for its

understanding a fairly intimate knowledge of the physiology of the neuromuscular system. The right time to impress its most important bearing on clinical medicine, how to detect its abnormalities, the reasons why such abnormalities give rise to symptoms, the variety of factors which influence it, is at the beginning of the clinical period, when physiology is still fresh in the mind of the student.

Before leaving the subject of orthopædics, there is one other aspect of it which I think requires emphasis on account of its great general educational value, and that is its close association with the Social Services of the hospital. A student should be given the opportunity of appreciating that we are as interested in the environment and soil from which Diseases and Dysfunction arise, as in their cure. Most cases of ill-health consequent upon poor muscle tone are social problems: maladjustments, malnutrition, overcrowding, poverty, fatigue, &c., and without the assistance of the Lady Almoner we are quite unable to help our patients. At present the student only sees this contact late in his career when clerking in the Departments of Psychology, Tuberculosis and Orthopædics, and even then its extreme importance is insufficiently stressed.

My theme throughout this paper has been that learning, like any other activity of the central nervous system, is a reflex action, a matter of external stimulus and response The ultimate aim of education is to awaken the higher intellectual centres and assist maturity. But, in the young, it is the lower mental centres which require our immediate attention, *maturity* can safely be left to look after itself. The best way to assist development is to avoid confusion by placing the student in an environment in which he can step by step educate himself, and I believe that, in the early forcing period, it is in the terrain of some of the specialties where the most suitable soil is to be found and the appropriate atmosphere most easily created.

If we have decided that certain subjects are fundamental to the study of medicine and are prepared to devote two or three years to them, it is folly not to make sure that these subjects become conditioned in the student's mind. This can be achieved without prolonging the training simply by rearranging the curriculum.

After the student has spent the first six months of the clinical period in departments which continually stress the important association of mechanics, anatomy and physiology to clinical medicine, he will be well grounded. By dint of constant repetition, from different angles and by different teachers, the reflexes will become conditioned, the fundamental subjects less likely to atrophy from disuse, then, he will be ready to broaden his foundation to include pathology and proceed to the study of disease.

Before we can persuade our general medical and surgical colleagues to allow us to take our proper place in the training of medical students, we must first try to persuade them to overcome their prejudice against us specialists. I cannot believe that they really object to specialism, and assume, that because a man studies a subject profoundly, he necessarily becomes narrow-minded; the reverse is the case, the more an intelligent person knows of one thing, the more he perceives its ramifications, the wider his horizon inevitably grows.

It has no doubt often happened, that on account of personal popularity, or other reasons, men, who failed to get on to the General Staff of their Hospital, because they did not quite come up to the standard, have been appointed in charge of a special department. Consequently, I believe, the idea has grown that specialists are intellectually second raters. How strong this factor is, it is hard to say, but, I suspect that subconsciously it plays a bigger part than either we or they realize. I personally have no objection to their holding such opinions. I am not arguing for myself or for you, only for specialism. If they feel their objections to us are valid, the onus lies with them to appoint specialists whom they can trust, and not on account of personal prejudice deny to specialism its logical place in the scheme of education.

On our side we too are to blame. We have not yet lived down the exuberance of youth. When struggling for advancement, there is a definite technique, and that is, to persuade the other fellow that you have something very special to sell. Our particular ware which we hawk around, is "orthopædic principles". I have studied orthopædics for twenty-five years, and have failed to perceive a single principle upon which our work is based, that was not taught to me by the Surgical Registrar, when I was a ward clerk. In reality we only employ general principles applicable to every branch of medicine and surgery. How can we ask to take a share in the general training of a student, when we talk of very special principles of our own? What we can claim, and with very good reason, is that we teach

general principles, and that we practise them on a larger scale in meticulous detail, and with amazing perseverance. That, I maintain, is our strongest claim for taking our proper place, which is at the beginning, and not at the end, of the clinical period.

If we are to play our part in any such reconstruction, we, particularly those of us on teaching hospitals, will have to reorientate ourselves. It will require a considerable amount of mental readjustment to change our position from that of a more or less post-graduate teacher to a muddled audience, already harassed by the prospect of approaching examinations, to one of a team of teachers of elementary surgery to eager young students. For the purposes of undergraduate teaching, we must seek to simplify our subject, we must get out of the "interesting case" complex, we must learn to extract interest from the commonplace, always to think of the student's intellectual development, always try to bridge the gap between what he already knows and what he is going to meet with in the immediate future. Moreover, I think we would do well to follow the tradition of the teachers of the pre-clinical period, where the heads of the departments themselves undertake the teaching of the fundamentals of their subject, and do not leave it to comparatively inexperienced assistants or registrars as occurs at present in the clinical period.

I trust the day will come, when all of us teachers will have a round-table conference to rearrange the curriculum upon more logical lines, and try to give it a more definite form, so that the student will the more readily perceive that it is all one continuous tale and not a cumbersome tome of short disconnected stories, some interesting and some dull.

I appeal to our general medical and surgical colleagues to elevate us from the status of short-story tellers, and allow us to contribute a few of the earlier chapters in that most thrilling of all narratives, "The Marvels of the Human Body".

The Conservative Treatment of Osteomyelitis

By K. C. McKeown, M.Ch., F.R.C.S.Ed.

Records of the use of sulphathiazole in cases of acute osteomyelitis are comparatively scarce. Those of Melton, G. (sulphathiazole in treatment of staphylococcal infections, *Lancet* (i), 274, 1941), Smith, A. L. (*Medical Times, New York*, **68**, 268, 1940), and Phemister (*Bull. New York Acad. of Med.*), may be mentioned. These papers, however, deal mainly with its use in the reduction of the primary mortality of the disease.

The object of this paper is to give a preliminary report of a short consecutive series of unselected cases treated with the drug.

The surgical treatment in all cases has been minimal, consisting of incision of the periosteum and drilling of the bone in the acute stage; and sequestrectomy, if required, at a later date.

The dosage of the drug was estimated as 1 g. of sulphathiazole per 20 lb. body-weight.

The cases fall into two groups.—In the first three cases to be described administration of the drug was commenced at the onset of the disease and was continued for eight days; a repeat course being given after an interval of three weeks.

In the other three cases administration of sulphathiazole began twelve to forty-eight days after the onset of symptoms.

Group I

Case I.—Boy, aged 10 years. Complained of pain over the lower end of the left femur for a day before admission to hospital. On examination the patient looked toxic. The temperature was 103° F. and the pulse 130. There was marked tenderness over the lower end of the femur and swelling of the knee.

Sulphathiazole was given at once in doses of 6 g. in the twenty-four hours and continued according to the plan already mentioned.

Operation was performed at the end of the second day. The lower end of the femur was exposed, the periosteum, which was thickened, was incised, and five drill holes were made in the metaphysis. Pus exuded from the lower four holes. A vaseline pack was inserted and plaster applied. The condition rapidly improved during the following five days.

Examination of the pus showed *Staphylococcus aureus* and a profuse growth was cultured.

Estimation of the blood sulphathiazole showed the concentration of the drug to be 7 mg.%.

X-ray at the end of one month showed commencing sequestration of a small area of the originally drilled cortex. The bone changes were minimal in extent.

Sequestrectomy was carried out after five months.

In this case the duration of treatment was six and a half months. On discharge the patient walked well with no limp. Flexion of the knee was almost full. The scar was soundly healed and has remained so.

CASE II.—Girl, aged 11 years. Complained of pain over the lower end of the left femur of two days' duration. Acute osteomyelitis of the lower end of the femur was diagnosed. A course of sulphathiazole was given and operation was carried out after six days. The periosteum was incised, and pus lying below it was evacuated. A single large drill hole was made in the shaft of the bone. The wound was packed with vaseline gauze and plaster applied.

Examination of the pus showed Gram-positive cocci, and culture yielded a scanty growth of *Staphylococcus aureus*.

Blood culture was sterile after six days' incubation.

X-ray examination after two months showed a small sequestrum, but otherwise bone change was minimal.

A small sequestrum was removed from the sinus after three months.

The patient was discharged after four and a half months' treatment. At this time the wound was soundly healed and movements of the knee-joint were only slightly limited (130°).

CASE III.—Boy, aged 9 years. Complained that, following an injury, he had pain in the region of the right arm. He was given a course of sulphathiazole and operation was carried out after ten days. A large abscess over the lower end of the right humerus was incised. The bone was not drilled. Subsequent treatment was carried out by the closed plaster technique.

X-rays taken after three weeks and further examination at eight weeks showed no bone change. The sinus was soundly healed at the end of four months' treatment and the boy has subsequently had no further trouble.

GROUP II

CASE IV.—Girl, aged 14 years. Complained of pain over the upper end of the left tibia and swelling over the knee-joint. The duration of symptoms before admission to hospital was two days.

Operation was carried out at the end of the second day. The periosteum was incised over the upper end of the tibia and four drill holes were made in the metaphysis. Pus exuded from all of these.

Culture of pus grew *Staphylococcus aureus*.

Sulphathiazole was not given until twelve days after the onset of the disease.

X-ray at the end of four weeks showed osteomyelitic changes in the metaphysis of the tibia. A sinus was still discharging over the upper end of the tibia after eight months but the wound appeared soundly healed three months later. At the present time there are arthritic changes in the knee-joint and flexion of the knee is limited to 90 degrees. The duration of treatment in this case was one year.

CASE V.—Girl, aged 11 years. History of a fall a week before symptoms began. She then complained of pain in the right knee and was unable to walk for a week. She was admitted to hospital and operated on two days later; that is, ten days after the commencement of the symptoms. The lower end of the femur was exposed and pus evacuated from the metaphysis by a single large drill hole. A course of sulphathiazole was not started until the twelfth day of the disease and a repeat course was given in six weeks.

X-ray at the end of three months showed extensive osteomyelitic changes in the lower third of the femur; and a further X-ray four months later showed that sequestration had taken place.

Sequestrectomy was carried out at the end of the eighth month, and a pedicle muscle graft inserted into the bone cavity. The wound was closed, and sound healing was obtained. The duration of treatment in this case was ten months.

CASE VI.—Boy, aged 10 years. He stated that he fell over a railing and injured his right thigh. Three days later he had very severe pain in the right thigh but he was not admitted to hospital until just under two weeks from the onset of the pain.

Operation was carried out and two large drill holes were made over the lower end of the shaft of the femur.

In this case sulphathiazole was not given until six weeks after the onset of the disease.

Examination of the pus showed that the infection was staphylococcal.

X-ray showed osteomyelitis of the lower half of the shaft of the femur. A further X-ray at the end of three months showed the formation of a sequestrum and the bone changes were more marked than in the previous cases, though still confined to the lower half of the femur. Sequestrectomy was performed at the end of eight months. At the time of discharge the wound was soundly healed; the range of movement at the knee joint was considerably limited. The duration of treatment in this, the last case of the series, was fourteen months.

Conclusion

In none of the six cases described was there spreading and gross bone involvement, but rather the destructive changes remained localized to a relatively small area.

The bone involvement in cases in Group I in which early administration of the drug was carried out was minimal, while in cases in Group II in which the drug was given at a later date the bone change was much more marked.

The duration of treatment averaged five months when the drug was given early, and eleven months when its administration was delayed.

In comparing the duration of treatment of this series of cases with similar cases treated at Queen Mary's Hospital during the past five years, before the advent of sulphathiazole, it was found that the duration of the disease was approximately halved.

I wish to thank Dr. W. Allen Daley for his kind permission to use the clinical material available at Queen Mary's Hospital, Carshalton.

Physiotherapy and the Soldier's Foot

By E. J. Crisp, M.B.

At every E.M.S. Orthopædic Centre a considerable problem is presented by the large numbers of soldiers with painful feet. Of these, only a minority have glaring defects, such as gross hallux valgus or rigidus, pes cavus with clawing of the toes, fixed valgus deformity secondary to spasmodic valgus or other similar conditions. These men have been placed in too high a medical category, and the only treatment advisable in the majority of cases is regrading or discharge from the Army, while of the remainder some may be improved by the orthopædic surgeon and others helped by the orthopædic bootmaker. Physiotherapy plays but a passive role; it alleviates, but cannot cure.

Fortunately, the type of case just described represents but a small percentage of those coming for treatment. The real problem is presented by the apparently normal foot which has broken down during military training. This type of case we see in ever-increasing numbers, and the absenteeism for which it is responsible must be causing the Army medical authorities much anxiety.

I am going to divide the cases into two groups, namely, Group A: feet which gave no trouble prior to joining the Army, and Group B: feet which, though more or less normal to look at, were already giving trouble in civil life. The majority of cases coming for treatment will be in Group B.

(A) the foot which was trouble-free prior to joining the army

Only a foot which is mechanically sound in every respect will stand up to the Army's vigorous system of training. Many a foot which in peace-time did all that was asked of it without complaint, nevertheless had certain inherent weaknesses which only came to light when it was subjected to greatly increased activity. The following types of foot are likely to breakdown:

(1) *The weak foot.*—The foot which we associate with a feeble physique, the foot with a deficient musculature due to a sedentary life, adolescence, overweight in early middle age, or following acute illness.

(2) *The stiff foot.*—The foot which is stiff as the result of inactivity, following a sprain, or as the result of assuming an abnormal posture on account of a painful focus. For example, the recruit with a plantar wart may march with his foot in varus in order to avoid pain. His foot will, as a result, ultimately become stiff.

(3) *The inco-ordinated foot.*—The foot in which individual muscle control is lacking, and which the owner uses not as a foot, but rather as a cow uses its hoof.

A recruit with feet subject to one or other of these defects is bound to crack up at a certain stage of his training, the contributing factor being ill-judged progression of his activities.

The Army boot.—I have not apportioned any blame to the Army boot, which is admirable for the normal foot. It is only the frankly defective foot which will be aggravated by its use. Soldiers with sound feet, without exception, all tell me that the Army boot is exceedingly comfortable. Moreover, when on leave they have found their civilian shoes rather uncomfortable and have been glad to return to their Army boots. Though soldiers with painful feet blame Army boots, what is really at fault is the Army's system of training.

The weak foot.—Acute fatigue, the direct result of making weak muscles work under

a full load, will cause many breakdowns. For example, a recruit who has never marched more than five miles is suddenly sent out for a twenty mile route march. His feet are completely exhausted, but before they have a chance to recover they are called upon for further activities the very next day. The consequence is that his feet never recover. In a case like this acute foot strain results, the feet will be valgus and exceedingly tender, there will probably be spasm of the intrinsic muscles and there may be some swelling. In addition, the condition of the feet will provide a suitable soil for the fibrositic nodule. The patient will complain of aching and throbbing even when at rest. There is only one thing to do; he is utterly exhausted; put him to bed until all pain, spasm and swelling have gone, the only treatment during this period being heat and massage. Strengthening and corrective exercises are then given for several days, the patient still remaining in bed. After this he is allowed to get up, strictly individual treatment is continued, and he is taught to stand and walk correctly. Only when all pain has disappeared and his feet are reasonably strong, is he promoted to the foot class. Later, when he has sufficiently recovered, he is sent for light P.T. and in due course he progresses to full P.T. and strengthening walks. He continues to attend the foot class throughout his stay in hospital, the physiotherapy department looking after his feet, and the sergeant-instructor keeping the rest of his body fit. This course of treatment will take upwards of six to eight weeks, but it is the only certain way of assuring that the recruit will return to his unit with his feet and body sound.

The stiff foot.—After a short time in the Army a stiff foot will become a painful foot. The foot will be called upon to work as it never did in peace-time, and, as it fatigues, adhesions and contractions will prevent the long arch flattening. Crippling pain will result and the soldier will be compelled to go sick. The treatment is eminently satisfactory. After a preliminary rest in bed, manipulation by the orthopædic surgeon is followed by heat, massage and exercises, still in bed, until bruising or reaction has subsided. Thereafter the soldier gets up and receives individual corrective, mobilizing and strengthening exercises from the masseuse, not being sent on to the foot class until his mechanics and mobility are normal. Subsequently the scheme is identical with that for the weak foot, but the time spent in hospital will be only four to six weeks. The final result will be excellent. Should the foot have become stiff in consequence of assuming an abnormal posture to relieve a painful area, in addition to restoring mobility, it will, of course, be necessary to deal with the primary focus.

The inco-ordinated foot.—The foot which is deficient in control of individual muscles, which is unable to dissociate synergists or to synchronize contraction and relaxation of opposing muscles will, under the stress of military training, become still more inco-ordinated, and this may ultimately result in the development of deformity. This will present a fairly constant picture; the foot will be in valgus, the transverse arch dropped, the toes clawed, and there may be some pronation of the fore-foot. At first glance the condition may be suggestive of spasmodic valgus, but examination will show that this is not the case, as peroneal spasm is totally absent. Pain will first be complained of under the metatarsal heads, later in the mid-tarsal joints and under the external malleolus.

We meet this type of deformity at every stage in its development, depending upon when the pain became sufficiently severe to cause the soldier to report sick. In an early case we notice that when the patient either stands or walks, his toes stick out straight ahead and may point upwards, because of excessive action of the long extensors, and that he is often unable to plantar-grade them. In fact, the appearance may give the impression of an hysterical foot. This state of affairs, if left untreated, will progress to clawing of the toes, which will occur when the lumbricals give up the unequal struggle. Ultimately, contractions in the long extensor tendons will complete the picture. The result will be best described as "pes valgus with claw toes." The great toe almost always escapes.

If we examine the recruit's foot in the recumbent position, we note the shape and the inability of the foot to relax. The patient would appear to be actively resisting, but experience suggests that this not the case, the rigidity of the foot being symptomatic of its inco-ordinated condition. With patience, total relaxation can be obtained and the foot passively restored to its normal shape.

One sees a large number of soldiers with varying degrees of this deformity, and many of them tell you that their feet were normal prior to joining the Army. It took me a long time to realize that they were speaking the truth; I could not imagine such a degree

of deformity occurring in so short a time, and blamed the recruiting boards for faulty grading. However, I am now quite satisfied that military training is responsible for the disability, but that it only occurs in feet which are inherently deficient in individual muscle control. Every foot which has broken down from this defect shows one constant fault, namely, its inability to dissociate the tibialis anticus from the long extensors of the toes. These two muscles, in addition to their other functions, act synergically in dorsiflexing the foot, but in every single case we shall find the long extensor of the toes grossly overacting at the expense of the tibialis anticus, whose action is either partly or completely suppressed. Presumably, fatigue plays a part in the production of this state of affairs, and it is worth pointing out that the extensor longus digitorum is at a mechanical advantage when the foot is turned out, and the tibialis anticus when the foot is turned in. In addition, pain in the transverse arch may provoke a "pain-withdrawal" phenomenon, in which the toes are powerfully hyperextended by the unintelligent reflex contraction of the long extensors.

Once we understand the mechanism by which this very interesting type of deformity is produced, it is comparatively easy to reverse the procedure and to re-educate the foot to normality.

After a preliminary rest in bed, the keynote of our treatment is to teach dissociation of the tibialis anticus and the extensor digitorum longus. This we do by training the patient to plantar-flex his toes while dorsiflexing his foot, and vice versa to extend his toes while plantar-flexing his foot. This I may say needs endless patience from the masseuse, full co-operation from the patient, and, of course, strictly individual treatment. As an additional measure we apply surging faradism to the tibialis anticus and the intrinsics, and, if contractions are present, passive stretchings of the toes will be necessary.

I have recently devised an improved method of muscle stimulation by which several individual muscles, in this case the tibialis anticus and the intrinsics of the foot, may be made to contract simultaneously and perform a definite action. The machine used is an "Indolor" and each muscle or group of muscles is supplied through a separate potentiometer so that each may receive an equal stimulus. The foot is attached to a footpiece which is hinged at the level of the metatarsophalangeal joints, the toes being tied down separately. The rear of the footpiece rotates on a swivel, the front of the footpiece slides to and fro in a horizontal slot, the result being that dorsiflexion of the foot produces plantar-flexion of the toes.

Two electrodes each are applied to the tibialis anticus and to the intrinsics. On surging the current, contraction of the tibialis anticus produces dorsiflexion of the foot, and by the attachment of the foot to the footpiece, plantar-flexion of the toes. Simultaneously, the stimulus to the intrinsics produces full lumbrical action. This is the precise movement we have been endeavouring to teach the patient and helps in re-education. At the same time our electrical stimulation strengthens the two muscles which are weak and, in addition, powerfully stretches the long extensor tendons and metatarsophalangeal joints, rendering any manipulation quite unnecessary.

By these various means this type of foot is re-educated, muscular tone and co-ordination restored, and deformities corrected. Then, and only then, does the recruit start class work and in due course P.T. After a stay in hospital of upwards of six weeks he will be fit to return to his unit, wearing his Army boots, and in his original category.

In theory, almost 100% of cases of the types which I have just described, should recover completely. In practice, our results are now approaching this figure. We have only achieved this by *rigorous observance* of the principles of preliminary rest, individual treatment, and a sufficiently long stay in hospital.

(B) THE FOOT WHICH WAS ALREADY GIVING TROUBLE IN CIVIL LIFE

The majority of people who suffered with their feet in days of peace, brought the trouble on themselves, a sedentary life, faulty posture, muscular inco-ordination or unsuitable shoes being mainly responsible. In other words, with the addition of faulty footwear, the same factors were in operation as those causing the pain-free foot to break down after joining the Army. In this case, however, the weak foot was already painful, the inco-ordinated foot already tending towards deformity, and military life has aggravated the condition.

The problem with which we are faced is thus very similar to that of the normal foot which has broken down during training. As, however, the condition will often have been

of fairly long standing, additional measures may be necessary, and in the presence of deformities surgical intervention will be called for. With these exceptions, the scheme of treatment is identical with that for the foot which was trouble-free before joining the Army, and the results should be equally good.

As regards deformities, after the orthopædic surgeon has corrected the hammer-toe or over-riding little toe, after he has dealt with claw toes by tenotomy or, in selected cases, by arthrodesis of the phalanges, after the chiropodist has excised all corns and callosities, then the stage is set for intelligent physiotherapy to play its part in returning the recruit to duty, his feet in better shape than ever before. This type of case offers plenty of scope for collaboration between the orthopædic surgeon and the physiotherapist, and, if sufficient time is allowed, the results can be brilliant.

Early hallux rigidus, in which bony changes are absent, can often be improved by treatment with hot wax, gently increased passive stretchings, and gently progressed resisted and active exercises, while any degree of elevatus of the first metatarsal is corrected by training the peroneus longus to plantar-grade the foot.

Fibrositis, which usually occurs in the plantar fascia, should be treated by infra-red and massage to localize the nodule, after which the injection of 1% procaine usually effects a cure.

The majority of cases of the types which I have just described should, after a full course of physiotherapy, be able to resume their military training in their original grade. Of course, we are bound to meet with disappointments, and among these will be the valgus foot secondary to a short tendo Achillis. If this shortening is considerable, neither raising the heel nor concentrated physiotherapy will avail, and regrading to a lower category will be necessary.

SUMMARY

There is no place in the Army for the soldier with painful feet, and our task is to return him to his unit in the shortest possible time with his feet so sound that there is no likelihood of their breaking down again. This can only be achieved by strict attention to the following points:

(1) The soldier with painful feet is suffering from a major disability which must be treated as such, and he must therefore be admitted to hospital. Out-patient treatment is unsatisfactory.

(2) In most cases preliminary rest in bed will be essential.

(3) Individual treatment is absolutely necessary until all mechanical errors are corrected.

(4) Sufficient time must be allowed in hospital for the soldier's feet to recover. This will take four to eight weeks. Allowing insufficient time will only result in failure.

(5) Full and intelligent co-operation from the patient is required.

(6) When up and about, Army boots should be worn whenever possible. "Slopping about" in plimsolls is harmful.

(7) The regimental M.O. should never regard a painful foot as a trivial complaint. He must realize that the sooner a case receives treatment, the greater the prospect of a satisfactory result.

A Case of Degeneration of the Intervertebral Disc Following Lumbar Puncture

By P. G. EPPS, M.B.

THIS case is very similar to those described at the last meeting by Mr. Everett (see Sect. Orthop., p. 208 this issue). The patient is a soldier, aged 27 years, who in May 1941 developed meningitis. During the course of treatment he had five lumbar punctures, the last of which was about July 25; this one took thirty-five minutes, and the patient describes pains shooting down each leg as repeated attempts were made to pierce the theca. At the beginning of August he was discharged, and went on leave; he had no pain at all then, but after fourteen days he developed, quite suddenly, a severe lower back pain, which he said caused him to collapse in about three days, and he was taken to hospital.

X-rays taken then, on August 25, showed no abnormality of the spine. The severity

of his pain was such that it was decided to immobilize him on a plaster bed. The pain grew worse, however, and at the end of September he suffered severe attacks coming on in spasms, lasting about ten minutes, of such acuteness that his pulse became feeble and his complexion paled. During the worst of these attacks, his abdominal muscles were rigidly in spasm.

X-rays taken on October 10 showed collapse of the intervertebral disc between the 4th and 5th lumbar vertebræ with absorption of the adjacent portions of the vertebral bodies.

FIG. 1.—Antero-posterior view showing diminution of joint space between L.4 and L.5.

FIG. 2.—Lateral view showing (*a*) diminution of joint space; (*b*) herniation of disc substance into the vertebral body of L.4; and (*c*) a large osteophyte growing from the margin of the body of L.4.

Since the end of September his condition has steadily improved. During his stay in hospital he has been afebrile, his blood sedimentation rate is 8 mm. in one hour, and his blood-count normal. The process appears to be aseptic degeneration.

I am grateful to Mr. Stamm and to Dr. Campbell, the Medical Superintendent of the hospital, for permission to publish this case.

The Technique of Arthroplasty

By T. T. STAMM, F.R.C.S.

IT is not the purpose of this paper to suggest any new method in the technique of arthroplasty, but to emphasize what the older surgeons clearly realized, namely, that the essential structures of the new joint—articular surfaces, synovial membrane, &c.—are formed, not at the time of the operation, but during the subsequent period of treatment. Arthroplasty is not an operation, it is a mode of treatment, the first stage of which consists in an operation for arthrolysis.

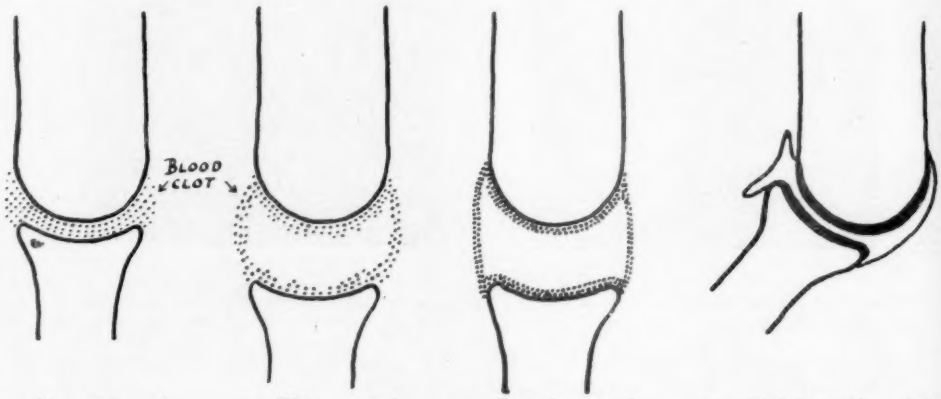
Most surgeons have had the opportunity of exploring a false joint which has formed

spontaneously following a fracture. It is found that the bone-ends are covered by a smooth glistening layer of dense white fibrous tissue, which forms an excellent bearing surface, while the surrounding fibrous capsule is lined by a very close imitation of synovial membrane, which does in fact secrete a glairy lubricating fluid. These structures can only have been formed by the organization of the blood-clot which lay between the broken bone-ends. The aim of the after-treatment in a case of arthroplasty should therefore be to endeavour to reproduce the conditions under which the blood-clot will tend to be organized in this way.

In the absence of direct confirmation by experiments on animals, the following scheme appears to me to be rational, and has in practice given good results.

The first essential is to limit the amount of blood-clot that is allowed to collect between the new joint surfaces and in the rest of the wound area. At the end of the operation, therefore, a firm dressing is applied, and the limb is immobilized without applying any traction. I believe this is a most important point. If there is much oozing from the bone-ends, a small drain may be left in for twelve hours to allow the blood to escape.

After forty-eight hours, traction is applied gradually, the maximum pull being achieved in three to four days. In this way the joint surfaces are slowly drawn apart without any fresh bleeding being caused. A layer of blood-clot may be expected to adhere to each of the rough bone surfaces, and as the gap between the bones widens, a space will appear between the two portions of the clot. This space will fill up with tissue fluid as it forms, provided that no fresh bleeding has been caused. The condition of the parts is now as depicted in fig. I, II.



I.—At end of operation. II.—First week after traction. III.—Fourth week. Blood clot organized. IV.—Eighth week. Joint surfaces consolidated.

FIG. I.

If traction is applied immediately after the conclusion of the operation, or is applied too rapidly, the whole of the space between the bone-ends will become filled with blood-clot, and its organization will be likely to lead to a fibrous, if not a bony, ankylosis.

Full traction is maintained for fourteen days before any movements are permitted. By the end of this period the clot will have become firmly adherent and will be commencing to be organized on its deep or bone surface. One movement daily in each direction may now be given, while traction is maintained manually, since there is now little risk of causing fresh bleeding, provided that the two surfaces are kept apart. These movements help to prevent the surrounding structures from becoming adherent. With this method of after-treatment, the full range of movement can often be attained easily and without pain on the first occasion that the joint is moved, though usually it is not wise to attempt so much.

After a further fourteen days it may be assumed that the clot has been organized into young fibrous tissue. A few movements daily may now be given with the traction

released, and the patient is encouraged to assist the movements actively. The new joint must not, however, be permitted to bear any load or strain at all. In this way the movements of the two joint surfaces on one another will mould the layer of young fibrous tissue on each articular surface before it has become too firm, so that two smooth and accurately fitting surfaces are formed. Traction is, however, still maintained in the intervening periods, to prevent the fibrous capsule, which is forming around the joint, from contracting.

After about six to eight weeks it may be assumed that this fibrous tissue is sufficiently mature to show little further tendency to contract, beyond the amount that can be prevented by gradually increasing periods of active, assisted exercises. The traction may now be discontinued tentatively, but if the range of movement should show any tendency to diminish, it must be recommenced at once.

The condition of the joint should now be as indicated in fig. 1, iv. The bone-ends are covered by a layer of smooth dense white fibrous tissue, closely simulating articular cartilage. The fibrous capsule is lax, permitting free movements, and the whole cavity of the joint is lined by synovial membrane secreting a glairy lubricating fluid, similar to that found in an adventitious bursa.

The joint is now fully formed, but is not fit to bear full body-weight or to take any great strain for at least another three months, since the internal structure of the bones themselves has to be remodelled to be able to withstand the altered stresses.

This method of after-treatment may be summarized and tabulated as shown in fig. 2.

First month	1- 2 days.	Immobilization without traction
	2- 7 days.	Immobilization. Traction gradually applied
	7-14 days.	Immobilization with full traction
	14-28 days.	Daily movements commenced, traction being maintained
Second month:	Traction released daily for active assisted movements	
Third month:	Traction discarded. Daily active assisted exercises	

NOTE.—Times suggested apply to the larger joints. In small joints these times may be considerably reduced.

FIG. 2.—After-treatment for arthroplasty.

The optimum time to be allowed for each step in treatment should, of course, correspond with the average times which it takes for the process of organization of blood into fibrous tissue to reach its various stages. The times given here are those which seem to be in keeping with what we know of this process, and they work out satisfactorily in practice. In the case of small joints where the amount of tissue to be organized is less, the times may be reduced without ill-effect. Once the initial reaction to the operation has subsided, the remainder of the treatment should, in most cases, be painless. Any complaint of pain by a reasonable patient is usually a sign that something is wrong.

A successful result depends entirely upon the most careful attention to detail and every step must be carried out either by the surgeon himself or by an assistant who understands the factors involved.

If after-treatment on these lines is to be followed, the operation itself should be as simple as possible. It would be irrational to interpose flaps of fascia or fatty tissues between the bone-ends, as is sometimes advocated. A layer of devitalized tissue of this nature could not possibly be expected to form a good weight-bearing surface; on the other hand it would be certain to interfere seriously with the proper development of the joint. The idea that it prevents the new joint from seizing up again is quite erroneous. With the technique of arthroplasty already described there is no difficulty whatever in preventing reunion occurring between the articular surfaces themselves. Failure to secure a reasonable range of movement is almost invariably due to fibrosis occurring around the joint. The interposition of fascial flaps cannot prevent this occurring—in fact, the reaction to its presence by the surrounding tissues might rather be expected to increase this tendency.

The operation itself should therefore consist in a simple arthrolysis, the bone-ends being carefully reshaped, and in the removal of any surrounding scar tissue or contracted ligaments that might interfere with movement.

The use of metal cups is, I believe, equally fallacious, if they are employed with the

object of preventing reunion of the bone-ends, for, again, this can be prevented without their employment, while they certainly do nothing to minimize the surrounding fibrosis.

I am not suggesting, however, that they may not prove to serve a useful function in certain arthroplasties. It appears to me that their function is twofold. First, to increase the area of the weight-bearing surface of the joint, when the bones themselves do not provide sufficient material for the purpose, and second, to distribute the weight borne by the joint more evenly over the whole articular surface, and so prevent excessive pressure being borne by any one part of it. I have tried to illustrate this in fig. 3.

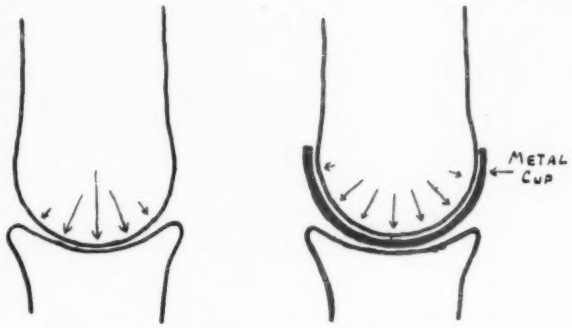


FIG. 3.—To show better distribution of pressure over articular surface afforded by use of metal cup.

I believe that treatment on the lines I have indicated would give a satisfactory result in every properly selected case if it were possible to control the extent of the surrounding fibrosis. While this method of treatment does, I think, tend to minimize the amount of fibrosis, this still remains a definite problem. It is proposed to experiment now with the use of deep X-ray therapy in small doses, on the analogy of its action on keloid scars, but an extended trial will, of course, be necessary before any conclusions can be drawn.

Excision of Both Femoral Heads in a Case of Ankylosing Spondylitis.—J. S. BATCHELOR, F.R.C.S.

S. H., male, aged 35 years.

This patient was first seen in 1938. His condition was unenviable, for both hips, the sacro-iliac joints and the lumbo-dorsal spine were ankylosed by bone as a result of ankylosing spondylitis which had commenced some years previously.

In March 1938 the head and neck of the right femur were freely removed. After-treatment consisted of strapping extension, with the leg at first in a Thomas's knee splint. At the end of the first fortnight hip movements were commenced; after eight weeks the splint was removed, and hip and knee movements were performed with the assistance of a sling beneath the knee. The patient left hospital at the end of fourteen weeks wearing a weight-relieving caliper with a moulded bucket, which was worn continuously for four months and then discarded during the next two months.

Although his condition was much improved and he could walk moderately well, the ankylosis of the left hip and spine made sitting impossible. Accordingly, in October 1938 the left femoral head and neck were excised, the after-treatment being the same as with the first operation.

He now has 90 degrees flexion, 25 to 30 degrees abduction, and a few degrees of rotation in each hip. All movements are painless. He gets about well with two sticks, sits comfortably in a chair and goes by car every day to work at an office. He has completely discarded the calipers, and, although there is obviously no real stability at the hips, there has been no appreciable increase in shortening during the past two years.

FIG. 1.

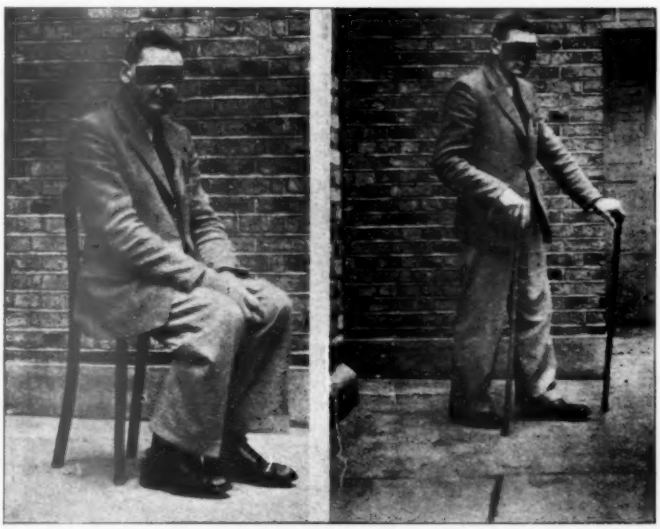


FIG. 2. FIG. 3.

CASE OF ANKYLOSING SPONDYLITIS.

Fig. 1 is a recent X-ray photograph of both hips, and figs. 2 and 3 show the patient sitting and standing.

Treatment of Fractures of the Shaft of the Femur.—J. S. Batchelor, F.R.C.S.

During recent years it has become a common practice to treat fractures of the shaft of the femur by means of skeletal traction through the lower end of the femur or upper end of the tibia, with the limb in a position of flexion at the knee.

I believe that this method is unsound and is responsible for many indifferent results.

There is no better splint for the routine treatment of fractures of the shaft of the femur than the Thomas's knee bed splint. This splint, when properly used with the leg straight, not only provides excellent immobilization, but also assists in the correction of deformities of alignment. With the knee flexed, these advantages are largely lost. The splint now acts merely as a cradle for the limb and its action in correcting axial deformities is much reduced.

Skeletal traction around the knee is open to many serious objections. A pin or wire through the lower end of the femur or upper end of the tibia passes through bone largely cancellous in nature, well covered with soft parts, and in close proximity to the synovial reflections of the knee.

These factors increase the risks of infection, and I have seen septic arthritis of the knee following traction in both situations, whilst delay in regaining movement at the knee and frequently permanent limitation of flexion are not uncommon complications of supracondylar skeletal traction. I think it is fair to say that in a straightforward case of fracture of the shaft of the femur skeletal traction through the lower end of the femur is completely unjustifiable.

When these fractures are treated with the leg straight it is possible to employ traction through the lower end of the tibia, and, in my opinion, this is a relatively safe area. Here the bone is largely compact and thinly covered with soft parts, and the synovial reflections of the ankle-joint are not involved.

I have encountered other minor difficulties when treating these fractures with the knee flexed. The pull on the shaft of the femur from a pin through the upper end of the tibia is indirect, and part of the force acts on the head of the tibia, pulling it forwards in relation to the lower end of the femur. If heavy or prolonged traction is used, this action may damage the ligaments of the knee and is a potent cause of knee stiffness.

With traction through the femur it is not uncommon for the lower fragment to be angled forwards; when this occurs it may be difficult to correct the deformity without transferring traction to a lower level.

In the majority of simple fractures of the shaft of the femur there is good callus union at the end of ten to fourteen weeks and rapid consolidation may now be produced by getting the patient up in a walking caliper. When the leg has been treated with the knee flexed, there may be some difficulty in getting full extension at the knee, and this delays the fitting of the caliper. This is a considerable disadvantage, for, quite apart from lengthening the period spent in bed, the stiff flexed knee throws a considerable strain on the fracture; and in the interval between taking the knee out of the Thomas's splint and fitting the caliper, whilst the patient is lying in bed exercising the leg, re-fracture may take place. This happened in two of my cases.

These difficulties with the flexed leg and with skeletal traction around the knee have led me to abandon this method of treatment, and I now treat all fractures of the shaft of the femur with the leg straight, with traction through the lower end of the tibia.

To get the best results it is essential for the surgeon himself to supervise the details of treatment. The initial reduction should be performed in the operating theatre. After insertion of the pin or wire through the lower end of the tibia, about three fingerbreadths above the tip of the internal malleolus, a Thomas's splint with a well-fitting ring is slipped over the leg, and manual traction is applied until approximately full length is obtained. The leg is then held in fixed extension by tying the stirrup to the end of the splint. A sling is placed below the site of fracture and, having been pulled tight so as to maintain the anterior bowing of the femur, fixed with two pins. This is the only sling that should be placed below the thigh. The leg below the knee is supported by slings fixed with clips, the knee being slightly flexed. The foot is held at a right angle with a footpiece attached to the splint. In the ward the splint may be slung from a Balkan beam, and a weight of 20 to 25 lb. is attached to the end of the splint over a pulley.

X-ray examination is carried out on the following day; any necessary adjustments are

made to the thigh sling, and the weight gradually reduced as complete reduction is obtained.

Daily quadriceps contractions are begun, but it is important that these should be given carefully during the first three or four weeks and until there is evidence of callus union.

At the end of six to eight weeks, if union is taking place satisfactorily, it is my practice to remove the pin or wire and apply strapping extension to the leg as far as the knee. Active knee movements over a limited range may now be begun. When the leg is taken out of the Thomas's splint, at the end of ten to fourteen weeks, active knee movements are practised in bed; in the majority of cases flexion to a right angle is obtained in three to four weeks.

SUPRA-CONDYLAR FRACTURES

These fractures, which are notoriously difficult to treat, form a separate problem. The characteristic deformity of the distal fragment is generally assumed to be due to the pull of the gastrocnemius muscle, and it is customary to treat these cases with the knee flexed. My limited experience has not convinced me that this position facilitates reduction.

I endeavour to lift the flexed lower fragment forward with a sling stretched between the bars of a Thomas's splint. There are two reasons why the flexed position of the knee hinders, rather than assists, this manœuvre.

Firstly, the length of the distal fragment available for leverage purposes is reduced by the backward gliding of the head of the tibia on the femur; and secondly, the depth of soft tissue below the lower fragment is increased by the relaxation of the knee flexors. Both these factors make it difficult to get a satisfactory purchase with a sling beneath the distal fragment.

Further, flexion of the knee brings the external popliteal nerve into a relatively more superficial position and makes it vulnerable to pressure by the sling. In a small number of cases treated with the knee flexed I have found it extremely difficult to get a satisfactory position, whilst pressure sores beneath the lower fragment, and damage to the external popliteal nerve, have occurred too frequently (Diagram I).

Diagram I.

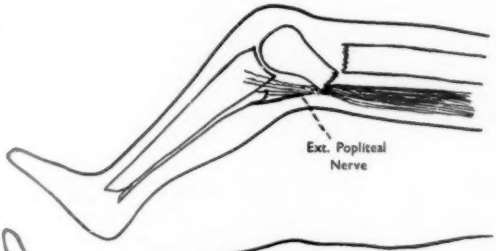
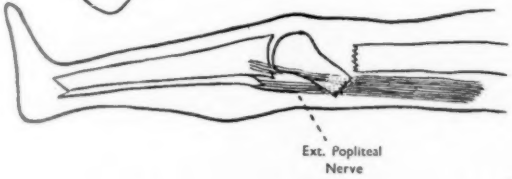


Diagram II.



I now treat all these cases in the same position as that used for the routine treatment of fractures of the femoral shaft. When the leg is splinted with the knee extended I have not found that the pull of the gastrocnemius presents any obstacle to reduction, whilst it is easier to get a satisfactory lift below the lower fragment, with less risk of pressure sores and damage to the external popliteal nerve (Diagram II). There is also the additional advantage that the knee is ready for a caliper immediately union has taken place. In a small number of cases treated by this method satisfactory results have been obtained.

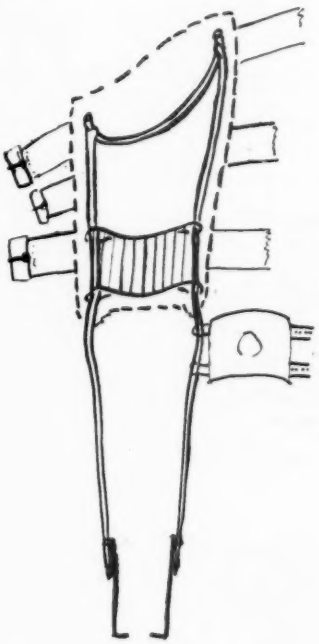
A New Walking Caliper

By W. H. Gervis, F.R.C.S.

The ordinary walking caliper as used in the after-treatment of fractures of the femur has certain disadvantages. It is expensive, it takes time to make, and unless it is a perfect fit it is useless.

This caliper is made from any old discarded caliper. The padding is removed and the front half of the ring cut away with a hack-saw. A piece of Cramer's wire, shaped to fit the back of the patient's thigh, is fixed across the caliper just above the knee by bending it round the side irons.

A wide plaster slab is then moulded on the posterior surface of the patient's thigh and the tuber ischii. The caliper is then placed in position over this slab and incorporated into it with several turns of plaster bandages. When set the plaster over the front of the thigh is cut away, the edges trimmed and 2-in. webbing straps incorporated.



The drawing shows the caliper with front half of ring removed, Cramer's wire in position, usual knee straps retained. Dotted line represents plaster of Paris moulded to fit posterior surface of thigh, with straps in position.

The caliper fits into the heel of the boot in the ordinary way, and is kept in position by the straps. It is weight-relieving and, in addition, supports the shaft of the femur when the patient is sitting. It can, of course, be removed for knee exercises.

Section of Ophthalmology

President—A. J. Ballantyne, M.D.

[*September* 26, 1941]

A Study of Mustard Gas Lesions of the Eyes of Rabbits and Men

By Ida Mann, D.Sc., F.R.C.S., and B. D. Pullinger, M.D.

Mustard gas (dichlorodiethylsulphide) was first used by the Germans at Ypres in 1917. At the time, the large number of casualties, the urgency of the situation and the absence of facilities for the minute examination of the eyes combined to account for the relatively rare and incomplete studies of the ocular lesion published during and just after the war of 1914-18. Interest in the subject dropped though occasional case-histories and speculations as to after-effects appeared between 1920 and 1935, but after that period interest again revived as it became clear that slightly mysterious cases of recurrent corneal ulceration were occurring among men subjected to relatively heavy doses of mustard gas ten to twenty years previously. The attention of one of us was first called to these cases of delayed mustard gas keratitis by Mr. T. J. Phillips, who collected a large number (70) at Moorfields with carefully recorded case-histories and detailed clinical and slit-lamp investigations (*Proc. Roy. Soc. Med.*, 1940, **33**, 229 (Sect. Ophthal., 5)). It was then apparent that a large gap existed in our knowledge of the progress of the condition. No records were known of the state of the eyes between the initial stage at the time of exposure and the subsequent onset of recurrent ulceration years after. The patients stated that they had been practically symptom-free during the interval, had continued in ordinary work and apparently suffered no visual disability. From the onset of the delayed keratitis, however, they experienced rapid deterioration of sight.

Since the subject of prophylaxis and treatment of mustard gas lesions of the eyes had again assumed great importance and since improved methods of examination (e.g. introduction of the slit-lamp) and facilities for experiment were available we decided to undertake an inquiry into the clinical pathology of the lesion based in the first place on animal experiment and secondly on laboratory accident cases.

The work falls into two sections, firstly, experiments on rabbits carried out at the Imperial Cancer Research Fund Laboratory by the kindness of the Council and the Director, Dr. W. E. Gye, and secondly, the correlation of the results of animal experiments with recent and late accident and war cases studied by one of us at the Royal London Ophthalmic (Moorfields) Hospital, and at various experimental laboratories where mustard gas is being handled at the present time.

Part I

The Pathological Effects of Mustard Gas on the Eyes of Rabbits

A strain of crossed Dutch rabbits with blue irides and a ring of pigmented conjunctival epithelium at the limbus is used for preference. Brown-eyed and albino rabbits are less suitable for observations of vascular changes in the iris and of epithelial healing.

Rabbits are suitable since they reproduce lesions almost identical with those seen in man, though they require a larger dose to do so. Their pathological processes are speeded up in proportion to their shorter expectation of life, and since the life of a rabbit is roughly one-tenth that of a man, a result which would take ten years to develop in a man may be obtained in a rabbit within a year.[1] It has thus been possible to study the genesis of delayed keratitis in eighteen months' work.

Rabbits show certain anatomical and physiological differences from man which are useful also from an experimental point of view. Their corneæ are relatively insensitive and their blinking reflex is often delayed for twenty minutes. It is therefore possible to keep the eyes open during long periods of observation without introducing complications due to abnormal drying of the cornea. The normal rabbit cornea usually shows a faint punctate staining with fluorescein from minute injuries with foreign bodies and from drying, but the epithelium is resistant and spontaneous ulceration or even conjunctivitis is rare. The possibility of infection is therefore not great and the induced lesions can be studied in their uncomplicated state. The greater area of the cornea relative to the sclerotic in rabbits makes them rather more suitable than is man for the study of corneal lesions and less so of combined conjunctival and corneal lesions. The fact that the vessels corresponding to the major circle of the iris are in rabbits visible through the cornea is also an advantage when observing early stages of iritis, while the palpebral aperture is sufficiently wide to allow of the examination of the limbus all round, which cannot be done in the smaller experimental animals such as guinea-pigs and rats.

We found by experiment that the sequence of events following the application of mustard gas to the eye varies very considerably with the technique of the application and that these variations are dependent on the anatomical site at which the mustard comes in contact with the eye, on the time it remains in contact and therefore on the size of the dose. It was therefore decided that a detailed study of the local lesion produced by a constant dose confined in turn to (*a*) the cornea, (*b*) the limbus, and (*c*) the lids and conjunctiva, would give more information than the application of varying concentrations to the whole eye and adnexa at once, although this also was studied when severe effects were required.

If every precaution is taken to ensure similarity of dose and accuracy of application the results obtained are of great constancy and suggest an inevitable chemical reaction rather than a biological response subject to individual variation. These results will be considered first with reference to anatomical site.

(I) THE UNCOMPLICATED CORNEAL LESION

Observations were made on 33 eyes in this group.

The rabbit is anæsthetized with ether and laid on its side. This is necessary on account of the peculiar oily consistency of liquid mustard, which tends to slide about on the eye under the action of gravity and which unless carefully controlled, may not exert its action at the apparent site of application. To see the liquid mustard more easily and thus control it, a small quantity of sudan black is added. This makes it visible on a blue eye and does not modify its action in any way. In the experiments which follow, the mustard gas used was an impure sample of the liquid. The lesions are thus likely to be comparable with those expected in man. The application is made with a glass rod having a small rounded end 0·25 mm. in diameter. The tip is dipped in the liquid mustard gas and applied lightly to the cornea without abrading the epithelium. From three to nine spots of mustard are used, arranged in a circle in the central area. The diameter of this circle should be less than two-thirds the diameter of the whole cornea, otherwise the limbus may become involved by spreading. The lids should be held open for fifteen minutes, either by hand or with a speculum. At the end of fifteen minutes the liquid mustard disappears, leaving a thin film of sudan black on the surface of each spot. This may be removed by touching lightly with filter paper or may be left. The eye is then allowed to close and the rabbit to recover. In some cases the rabbit was not anæsthetized and the application did not appear to be painful. The sequence of events was then studied in detail.

[1] This calculation is based on observations made on spontaneous cancer in man and animals and on the induction of cancer by means of carcinogenic agents. It can be shown also that this rough proportionality exists in healing lesions. It has been borne out in the present paper.

Observations.—Day of application: The liquid mustard tends to slide unless the centre of the cornea is maintained in an upward facing position for four minutes. After four minutes there is practically no tendency to slide. The small droplet is at first hemispherical and projects from the surface of the cornea. After about a minute it often changes its shape, puts out pseudopodia and begins to slide. From observations on sliding droplets it is possible to say that contact for two to three seconds is sufficient to destroy the epithelium. If a droplet remains in contact for longer than this it begins to penetrate the substantia propria. It reaches Descemet's membrane and endothelium in two minutes. In 6·5 minutes (average) it has passed through the cornea and the aqueous and has reached the iris where it produces localized hyperæmia. In most cases the hyperæmia gradually spreads to involve the whole iris. In four minutes none of the droplet remains on the surface. If droplets be placed over a sector of the iris and not in the centre of the cornea the small radial vessels running from the major circle towards the pupil will be seen to flush first (fig. 1, Plate I). After a few minutes more the larger vessels running peripherally from the major circle dilate also. This flushing of the iris may persist as an iritis lasting some days accompanied by aqueous flare and occasionally there is a true exudate in the anterior chamber.

As the droplets soak into the cornea they appear to dig little pits in the epithelium into which they gradually sink. Abundant clear or milky tears[1] are poured out immediately.

If fluorescein is dropped into the eye within a few minutes of the application of the mustard there will be no staining. In a quarter to half an hour the points of application are stained, but nothing else. As the effect of the mustard spreads the stained areas increase so that at twenty-four hours there is a large central stain embracing all the spots of the application. This may increase further up to forty-eight hours, though it usually begins to heal at about thirty hours.

There is no immediate change in transparency of the cornea and in unanæsthetized rabbits the application does not appear to be at all painful. After some hours the eyes look a little watery and there is some hyperæmia of the conjunctiva. There is no visible change in the substantia propria on the first day. Slit-lamp examination reveals damage to the endothelium which shows a "beaten silver reflex".

After twenty-four hours: The conjunctival hyperæmia has increased slightly, but there is no discharge, beyond occasionally a little dried mucus at the inner canthus. The lids show no abnormality.

The area of staining in the centre of the cornea is circular and includes all the spots of application. Occasionally the exact sites of the droplets can be seen as small greyish dots within the stained area. The stain penetrates the whole thickness of the cornea more rapidly than normal and diffuses into the aqueous in from three to five minutes.[2] The greyish areas (i.e. the worst affected) often take up the stain less well than the region just surrounding them (fig. 2, Plate I). The area involved therefore shows a central region over which the epithelium is destroyed and within which there are denser grey spots marking the sites of the droplets. The large area of destruction of the epithelium is due probably in part to spread of the mustard by soaking into the tissue in all directions and partly to a vapour effect from evaporation of the droplets during the time in which they are on the surface.

The epithelium surrounding the staining area is œdematous (epithelial bedewing) and if the diameter of the stained area is two-thirds that of the cornea this bedewing will extend to the limbus. Otherwise the edges of the cornea will be normal.

The substantia propria of the cornea is now no longer transparent, but shows a greyish haze in the central region. This is due to œdema which separates the fibres and gives a very characteristic slit-lamp appearance of dark (optically empty) spaces outlined by irregular fluffy whitish partitions (fig. 3, Plate I). This appearance is most conspicuous in the superficial third of the substantia propria. The cornea may be swollen to twice its normal thickness or more in severe cases.

[1] The milky secretion appears to well out from under the third eyelid and is probably Harderian.

[2] If the epithelium is mechanically removed from a rabbit's cornea and fluorescein dropped in, the stroma is stained half-way through in five minutes, all through in ten minutes and in twelve minutes the endothelium is stained and the colour begins to appear in the aqueous.

The endothelium may be completely destroyed in the centre of the lesion or may show a disturbed reflex like beaten silver.

At two days, the staining area is usually smaller, but the endothelial disturbance and the œdema of the substantia propria are worse. There is a zone of epithelial bedewing around the staining area, and beyond that single hydropic cells can be seen here and there in the epithelium some distance away. These cells, seen as single, bright, shining points are also characteristic of recent lesions of moderate severity in man. There is no discharge.

At three days there is still slight conjunctival hyperæmia, but no discharge and no abnormality of the lids. There may be a small central staining area, but in the smaller lesions this has usually disappeared, and the epithelium is intact though still bedewed. The œdema of the substantia propria is lessening and as it subsides the cornea returns to its normal thickness but not to its normal texture. Instead of its usual homogeneous and slightly speckled appearance it now shows a series of thin shiny curved lines, running in all directions and looking rather like fibrils of floss silk scattered throughout the thickness of the cornea (fig. 4, Plate I). This "silkiness" is best seen in the broad beam of the slit-lamp. In the narrow beam the cross sections of the silky lines show up as scattered bright dots and short, shiny, stratified lines. Silkiness is first seen on the third day in a zone, round the centre of the lesion, where the œdema is subsiding. As this subsidence continues the silkiness increases until the whole of the central area shows it. The endothelial disturbance is still present, but the area of destruction is lessening.

At four days there is no staining of the epithelium and the bedewing and œdema are less. The lesion can be resolved into three concentric zones. The centre shows some œdema of the substantia propria. Surrounding this is an area of "silkiness" which corresponds to the area of endothelial disturbance and outside this again is the outer edge of the area of epithelial bedewing. Thus the largest circle represents the area of damage to the epithelium, with a smaller zone within it in which the substantia propria and the endothelium are altered. The endothelium can be seen regenerating at the edges of the patch of destruction.

The lesion is therefore practically quiescent at four days. The œdema continues to subside and its place is taken by the silky appearance.

At seven days there is no œdema and only slight epithelial bedewing in the centre. The silky change is well developed and the endothelium still shows a disturbed reflex. The eye looks perfectly quiet and normal to macroscopic examination. The silky change if excessive may show as a very faint nebula in certain lights, but is difficult to see without a slit-lamp. It appears to be more or less permanent though in the course of months it becomes less marked. The endothelial disturbance disappears completely in time and is usually gone at eleven days. The epithelial bedewing lasts the longest and may persist in the centre for several weeks (up to five in a nine-spot lesion). In man it lasts much longer and there is some evidence that it may be permanent though very slight. Isolated hydropic cells can be detected for a long time in both man and rabbit, after the eyes look absolutely normal to superficial examination.

The appearance and course of this central lesion affords a striking example of some of the physical and chemical properties of mustard gas. That the liquid penetrates with remarkable rapidity is shown by the fact that it passes through the cornea and aqueous in six and a half minutes. It is, as it were, soaked up by the cornea and spreads widely within it and throughout the deeper structures also until it has become sufficiently diluted or broken down to cease to act. On its passage through the cornea it changes the fibres, and kills epithelium, corneal corpuscles and endothelium. The epithelium and endothelium are replaced by cells from beyond the lesion, but the substantia propria, though permanently altered, is not cast off as a slough, and after a brief period of œdema, returns to its normal thickness though it still shows a pathological change which may be permanent. Since the cornea is not vascular we can thus see the action of the mustard on a tissue uncomplicated by coincident disturbance of circulation, except at the limbus where there is slight hyperæmia. It is interesting to note that even in the absence of capillaries, œdema is a prominent feature of the lesion.

(2) THE LESION INVOLVING THE CORNEOSCLERAL JUNCTION

The lids of some rabbits were held open with a speculum. Other rabbits were anæsthetized. Five to nine droplets were applied to a sector of the cornea in the shape

of a V with the ends of the two limbs on or near the limbus. The treated eyes were kept open for fifteen minutes after the application, in all cases except those in which the speculum accidentally fell out. In this way a certain variety of lesions was produced; in some cases all the nine spots were effective, in others, some of the spots were not as large as others and in some the third eyelid brushed over the cornea before fifteen minutes, or the lids partially closed. Thus it was possible to study a series of lesions, varying from a pure corneal and corneoscleral lesion to one of moderate severity involving the third lid or the margin of the upper lid as well. A further series of experiments to be dealt with later, was done, using a single measured drop placed on the cornea, the eye being allowed to close immediately, so that the drop spread to the cornea, limbus, ocular and palpebral conjunctiva and the lid margins.

(i) *Sectorial lesion of moderate severity.*—51 eyes were observed in this group. Not all the rabbits were anæsthetized. The spots (five to seven) were placed in a V-shaped area at the upper part of the eye, the apex of the V at the centre of the cornea and the two limbs on the corneoscleral junction (*see* fig. 1, Plate I).

Observations.—At the time of application the eyes water slightly but there does not appear to be pain in the unanæsthetized animals. In about six minutes the section of the iris underlying the V becomes hyperæmic, the radial vessels running towards the pupil first and then the larger vessels peripheral to the major circle (fig. 1, Plate I). In ten minutes the conjunctiva at the limbus becomes slightly swollen. In two to three hours there is a small fleck of mucopus at the inner canthus, the conjunctiva in the sector of application is more swollen and the spots stain individually. The hyperæmia of the iris vessels spreads so that the whole iris is engorged in five hours. In six hours there appears to be slight photophobia and the eyes are kept half shut. In seven hours the slit-lamp shows an aqueous flare (=increased albumin content of aqueous). The corneal changes are as described above.

In one day the eyes are open with slightly drooping lids, conjunctivæ are hyperæmic and flakes of mucopus are found at the inner canthi. If this discharge dries on the fur of the lower lid it may produce a mechanical ectropion which disappears on washing the lid. The whole of the sector of application, not only the spots, now stains with fluorescein and also the œdematous conjunctiva at the limbus opposite it. The stain on the conjunctiva is orange, that on the cornea green and shows unusually rapid penetration, apparently due to damage to the stroma (substantia propria) allowing the dye to soak through. If the epithelium is mechanically removed from the rabbit's cornea and fluorescein dropped on, the colour begins to appear in the aqueous in twelve minutes, but in the mustard gas injury the fluorescein passes into the aqueous in from three to five minutes.

There is destruction of epithelium in the staining area and bedewing over a wide area but not over the whole cornea. The substantia propria in the sector is œdematous (primary œdema) and the spots of application may look denser than the rest as in the central lesion described above. There is the endothelial disturbance previously described or destruction. The pupil may be sluggish and there is hyperæmia of the iris and an aqueous flare. In some cases a gelatinous exudate can be seen coming from the sector of the iris corresponding to the sector of application.

In two days there is still slight mucopurulent discharge and where it sticks to the fur this tends to fall out, but the lids are not glued together, though they may be slightly swollen. The epithelium is beginning to cover the denuded area by sliding from the healthy parts. This can be seen in brown and blue eyed rabbits as the pigmented conjunctiva at the limbus slides over the cornea carrying the pigment with it (fig. 5, Plate II). This pigment slide begins in about forty hours and continues for three days, i.e. until the epithelium can no longer be stained. The new areas of epithelium show bedewing. The substantia propria is more œdematous in the sector and just beyond, but the penetration of fluorescein is not quite so rapid. The iritis is subsiding.

The conjunctiva at and between the points of application at the limbus is œdematous, quite white and no blood-vessels can be seen in it. There is usually a line of hæmorrhage at the limbus and sometimes above the pale area. The surrounding conjunctiva is hyperæmic.

In three days the staining area is less and the discharge is clearing up, unless the lids have been accidentally touched when it persists longer. The corneal œdema has increased

slightly, and the migration of pigmented epithelium has progressed. The œdema is mostly of the superficial third of the cornea.

In four days: As a rule the staining has almost or completely disappeared (as in the central lesion) and the pigment is scattering over a wider area and disappearing. The œdema of the substantia propria is less and is confined to the sector. In the conjunctiva there is increased capillary activity at the margins of the pale area and the limbal loops on either side of it are engorged. The eye on the whole looks better.

In five days there is no stain, practically no discharge and the œdema is much better, though still present in the sector just at the limbus. The conjunctiva is not hyperæmic except just at the limbus at the edges of the pale patch where the limbal loops are active. The iritis has disappeared.

In six days the eye looks macroscopically quite quiet except for a very faint haze above. The œdema (primary œdema) has practically disappeared but the slit-lamp shows great activity of the conjunctival vessels at the edges of the pale area (fig. 6, Plate II). If the eye is observed only until this stage it would be passed as practically cured, and so far the course is that of the pure corneal lesion except for the damage to the vessels at the limbus.

In nine days, however, a marked change for the worse is apparent. The conjunctival vessels are beginning to invade the cornea at the edges of the sector, not only superficially, but also at all levels, most of them being about one-third the way through. These invading vessels are accompanied by a considerable increase in the œdema of the substantia propria (secondary œdema) which just precedes them and spreads through the sector as the vessels advance. The rest of the conjunctiva is not hyperæmic and there is no fresh discharge but the cornea begins to look worse.

In eleven days the invading vessels are well established and the secondary œdema is considerable. The appearance is often like the typical "salmon patch" of interstitial keratitis in man with the difference that although the vessels in the cornea are at varying depths they all originate from the superficial conjunctival vessels and not from scleral branches. The advancing capillaries are peculiar and their distribution characteristic. They grow in as fine straight vessels with tapering ends which do not yet curve round to make a return channel. Close observation with a slit-lamp magnifying 25 times fails to reveal any movement of the blood in these tips which are packed close with corpuscles. The ends often branch at right angles, or right-angled branches occur nearer the source of the vessels. The blood appears to clot in many of the tapering ends; intracorneal hæmorrhages spread out from them; hæmolysed blood can sometimes be seen seeping along the corneal fibres. More often the tapering ends of the vessels become detached. This is usually followed by the formation of a channel for a return supply at the proximal end. Some of the invading vessels have bulbous ends and assume fantastic shapes, detached points, branches and islands of blood being constantly formed, disappearing and reappearing rapidly, the whole pattern varying from day to day, always extending farther into the cornea, and always accompanied by secondary œdema (fig. 7, Plate III). The patterns assumed by these invading vessels suggest that they are growing unchecked into spaces formed by splitting apart by œdema of altered corneal fibres. Their arrangement is not unlike that of the so-called Bowman's canals, an artefact produced by splitting a cornea by forcing air into it, which show the same bulbous ends and right-angled branchings. On the other hand their arrangement often differs entirely from that of blood-vessels grown experimentally in the transparent Sandison-Clark chambers in the rabbit's ear. The vascularization spreads and increases from the eleventh to the thirtieth day or longer. The pale area of conjunctiva (which has been killed) is invaded by regenerating vessels which in turn spread to the cornea, but the first and greatest invasion is from the edges of the sector, through the uninjured limbus. Most of the vessels lie one-third the way through the cornea. After thirty to thirty-five days the supply vessels begin to narrow, the circulation slows, the tapering ends disappear and the remaining vessels narrow down and gradually become more regular. The œdema subsides simultaneously. The pigment line which is broken at the limbus may partially reform. The pigment scattered on the surface of the cornea disappears and the eye begins to improve again. As the corneal œdema subsides the silky appearance mentioned in the pure corneal lesion becomes visible throughout the greater part of the sector.

By about the sixtieth day or less the secondary œdema has all cleared up leaving only the silkiness, which is more or less permanent: that is to say, it has disappeared after

more than a year in a few rabbits. The hæmolysed blood disappears as do many of the vessels. Those remaining become fine and regular in arrangement and are often empty. They can be made to fill up temporarily by gently rubbing the eye through the closed lids. Slight changes such as endothelial disturbance, faint pigment speckling and faint epithelial bedewing may persist for three months. Indeed slight epithelial bedewing and Hassl-Henle bodies on the endothelium may remain almost indefinitely. Such an eye, however, does not seem in danger of relapse.

(ii) *Sectorial lesion of greater severity with slight lid involvement.*—Thirty-nine eyes were observed in this group. If nine spots are applied and the limbus and conjunctiva slightly more injured than in the preceding series, as well as possibly a small area of the lid margin or the third lid, the course of the process is lengthened and various further changes occur. These can be classified as: (*a*) Increased discharge. (*b*) Recurrent thromboses. (*c*) Formation of blood islands. (*d*) Deposition of cholesterin and fat. (*e*) Persistent œdema, formation of fibrous tissue and cellular infiltrations.

(*a*) *and* (*b*). *Increased discharge and recurrent thromboses.*—The lesion is at first similar to one of moderate severity except that the discharge persists longer, especially if the third lid has been injured. The œdema of the substantia propria, both primary and secondary, involves not only the sector of application, but the whole cornea, and the newly formed vessels are more exuberant. The clearing up of the primary œdema at the end of the first week is not so complete. The condition begins to clear up at about sixty days as before, but instead of steadily subsiding it shows exacerbations about every fortnight after that, with fresh ingrowth of vessels, increase of œdema and thromboses and intracorneal hæmorrhages which begin to clear up again and then recur. These events may continue for six or nine months or more, and then finally cease, the vessels narrowing and the œdema subsiding but probably relapses are always possible since many vessels remain in the cornea.

(*c*) *Blood islands* (fig. 8, Plate II).—In some lesions similar to those described above the intracorneal hæmorrhages take the form of large blister-like collections of blood, usually in the most superficial layers of the substantia propria. The vessels of supply constrict and disappear but the "blood islands" remain for many months. There appears to be no great stimulus for their removal, such as exists in connective tissues.

(*d*) *Deposition of cholesterin and fat.*—In some instances of severe vascularization especially if there is one large vessel of supply arborizing freely towards the centre of the cornea, the regression of the vessels at about three to four months may be accompanied by the deposition of cholesterin crystals, first outside the vessel walls and later over the whole area previously occupied by them. As the vessels retrogress the cholesterin is left behind often in the form of a semilunar glistening opacity with its concavity towards the main supply vessel (fig. 9, Plate IV). Fatty degeneration visible with the slit-lamp as opaque, flocculent, white masses may follow the cholesterin and both may be present together. The eye may be fairly quiet after six to seven months. If it be watched, however, it will be seen to break down again in about seven to eight months, the cholesterin apparently working up to the surface, causing ulceration of the epithelium and being cast off with loss of substance so that a small pitted scar is left. The fatty degeneration also may lead to recurrent secondary ulceration. These eyes continually heal and break down, each small ulcer staining for about four days. In some cases, however, the cholesterin is deposited in the deeper layers near Descemet's membrane where it does not cause secondary ulceration and remains unchanged; in others it disappears without ulceration.

(*e*) *Persistent œdema and formation of fibrous tissue.*—When the eye and lids have been more severely injured and the discharge has been greater and more prolonged, there may be no tendency for the œdema to clear up (fig. 10, Plate IV). The primary œdema may merge with the secondary œdema and the whole cornea may become completely waterlogged and enormously swollen up to twenty times its normal thickness. This may persist, with repeated thromboses and exuberant vascularization for months. Large blister-like collections of fluid form among the superficial fibres of the substantia propria and occasionally though not often between the epithelium and Bowman's membrane. The surface becomes irregular, corrugated and thrown up into ridges and circular blebs. In these the corneal structure is entirely replaced by very vascular fibrous tissue which may invade the larger part of the cornea. These œdematous thickened fibrous corneæ never clear and show a great tendency to secondary ulceration and to surface keratinization. Large

superficial ulcers may occur after about seven months (fig. 11, Plate V). They may take a week or longer to heal and then break down again. They are much larger and more persistent than the small ulcers associated with cholesterin noted above. Some of these corneæ have been observed for nine or ten months and show no tendency to stabilize or resolve.

In some cases the blisters and blebs become filled with pus and indeed in all these severely injured eyes there is persistent discharge. How great a part infection plays in keeping up the œdema is not yet clear, but it seems likely to be of more importance in cases where the lids are injured severely as well as the cornea and limbus.

(3) SEVERE LESION OF THE WHOLE EYE AND LIDS

Fifteen eyes were used in this group. If a large measured drop (approximately 0·0005 c.c.) be placed on the cornea and the eye allowed to close, a generalized lesion of great severity is produced. The reaction is too great to study the early stages in detail. For the first nine days the eyelids and ocular and palpebral conjunctiva are so swollen and œdematous that it is impossible to see the cornea. There is copious discharge which glues the lids together and mats the fur and causes it to fall out over a wide area around the eye. As the swelling decreases and it becomes possible to see the eye, the lids become notched or "ruffled" and everted so that the lower lid especially is not properly in contact with the globe and is constantly covered with discharge.

The corneæ are richly vascularized and excessively œdematous. Necrosis of the cornea may be so extensive that in two and a half to three months the substantia propria will appear to deliquesce and disappear over a large or small area, giving rise to a descemetocœle which eventually ruptures, with collapse of the eye, infection, panophthalmitis and finally phthisis bulbi with a shrunken globe, deformed lids and chronic discharge.

COMMENT

These possibilities can be tabulated (*see* Table I). They correspond very closely, though much condensed in time, with the lesions seen in man, including the "delayed keratitis" still affecting men exposed to mustard gas in the last war. Œdema, persistent epithelial bedewing, nebulæ and silkiness, vascularization, recurrent thromboses and intracorneal hæmorrhages, curiously shaped vessels, blood islands, cholesterin, fat, recurrent ulceration, perforation and phthisis bulbi have all been observed in man so that there seems good ground for supposing that the experimental lesion in rabbits produced by droplets is comparable to the effect of fairly severe exposure to vapour in man.

The majority of these pathological changes may be produced by agents other than mustard gas. The most characteristic signs are the blood islands and the peculiar varicosities seen after subsidence of the acute stage, also the ulceration of the superficial cholesterin deposits in the absence of fat. So far these signs have not been produced in rabbits by any other means, nor observed in man in conditions other than mustard gas keratitis. The diagnosis rests on a combination of the non-specific lesions with the typical vascular and degenerative changes in a definite time relationship and at a definite anatomical site. The lesions in man are described in the next section.

In conclusion we wish to thank Group Captain P. C. Livingston, Flight Lieutenant H. M. Walker, and Messrs. Glaxo for their collaboration in handing over to us their collection of rabbits for a study of the late lesion in their series as well as our own.

PART II

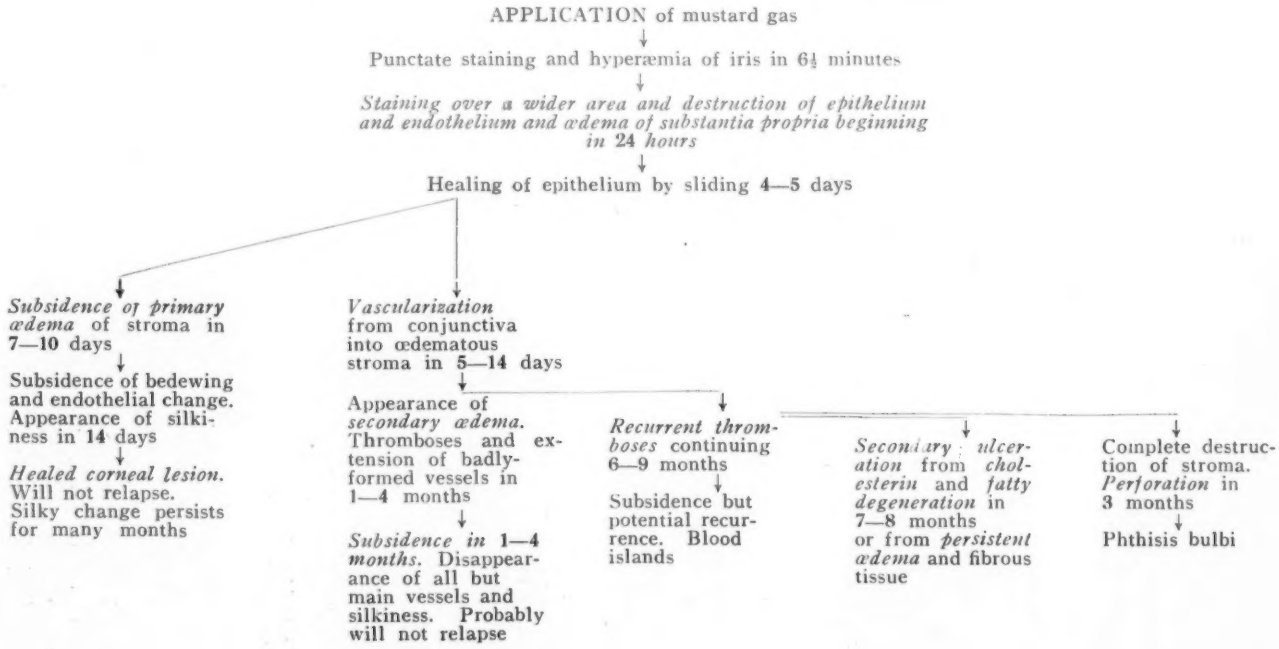
STUDY OF THE CLINICAL PATHOLOGY OF MUSTARD GAS INJURIES TO THE EYES IN MAN AND ITS CORRELATION WITH THAT SEEN IN RABBITS.

By IDA MANN, F.R.C.S.

A sufficient number of cases of mustard gas injuries to the eye in man were available for the correlation of the changes with those in the rabbit. Allowing for slight anatomical differences which modify the appearance somewhat in rabbits, the similarity is remarkably close.

I am deeply indebted to Drs. MacLaren-Ferrie and Chiesman for their valuable help and close co-operation in collecting and observing the recent cases, to the late Mr. Bernard

TABLE I.—COURSE OF MUSTARD GAS LESIONS OF RABBIT CORNEA COMPILED FROM OBSERVATIONS ON 138 EYES.


APPLICATION of mustard gas
Punctate staining and hyperæmia of iris in 6½ minutes
Staining over a wider area and destruction of epithelium and endothelium and œdema of substantia propria beginning in 24 hours
Healing of epithelium by sliding 4—5 days
Subsidence of primary œdema of stroma in 7—10 days
Subsidence of bedewing and endothelial change. Appearance of silkiness in 14 days
Healed corneal lesion. Will not relapse. Silky change persists for many months
Vascularization from conjunctiva into œdematous stroma in 5—14 days
Appearance of secondary œdema. Thromboses and extension of badly-formed vessels in 1—4 months
Subsidence in 1—4 months. Disappearance of all but main vessels and silkiness. Probably will not relapse
Recurrent thromboses continuing 6—9 months
Subsidence but potential recurrence. Blood islands
Secondary ulceration from cholesterin and fatty degeneration in 7—8 months or from persistent œdema and fibrous tissue
Complete destruction of stroma. Perforation in 3 months
Phthisis bulbi

Chavasse for allowing me access to his cases, and to Mr. T. J. Phillips for permission to use his cases and detailed unpublished work, on the late stages of the lesion, which has been necessary to complete the picture.

Although observations on the recent accident cases are still continuing and certain gaps exist in the human series, it is possible to say that:

(1) The pathological process is similar in man and the rabbit, the time relationships of the various stages being comparable, taking the accepted standard that a rabbit's life is one-tenth that of a man and its reactions therefore ten times as fast.

(2) That the reaction (acquired sensitivity apart) in man as in the rabbit is dependent on the size of the dose and the anatomical situation.

(3) That the explanation of the "late keratitis" seen in man up to twenty years after exposure has been attained by observation of the lesion in rabbits.

The human cases can be divided into five groups depending on the severity of the lesion.

GROUP 1.—EXTREMELY MILD CASES. CONJUNCTIVA ALONE AFFECTED

Ten cases fell into this group. They were examined at varying times after the accident from nine days to two years. Most of them were wearing either eye shields, chemical goggles or respirator at the time of the accident, which in some cases was a direct splash, in others exposure to vapour. The amount of protection afforded even by the Army eye shield appears to be considerable.

Three of the cases were unaware that they had been exposed until the onset of symptoms. The usual history, however, was that the eyes became slightly bloodshot and the lids slightly swollen a few hours (usually not more than six hours) after known exposure. Complaint was made of a feeling of irritation, but there was very little mention of photophobia and the eyes were never closed. The feeling of soreness lasted usually four to seven days, but the patient did not stop working. In some cases the irritation was said to have lasted some weeks, but nothing could be seen to account for it.

In none of the cases examined in this group was there any corneal abnormality due to mustard gas.

The earliest case seen was at five days. The patient had also had an erythema of the neck which was still just visible. The eyes showed hyperæmia of the conjunctivæ but no hæmorrhages or anatomical disturbance of vessels. This was all that was ever seen in cases in this group.

Two of the cases are instructive. They both had a history of a splash and in each case the eye was washed out very efficiently and copiously (in one for twenty minutes) within less than a minute. One used bicarbonate of soda lotion first and then tap water, the other tap water only. In one case the fingers of the man who washed out the eye were burnt as were the patient's lids. In both the lids were very swollen and the eye closed the next day, suggesting a severe lesion, but when the eyes could be opened, in four days, it was found in both that the cornea had escaped completely, although there was intense conjunctival hyperæmia. On the thirteenth day, in one patient, the skin of the lids showed hard dry sloughs, but the eye was open and the cornea absolutely normal, in spite of the fact that the lower fornix and lower half of the ocular conjunctiva were intensely hyperæmic, making it certain that some mustard (either vapour or liquid) had actually entered the eye. The other case had occurred two years previously and at present the cornea shows no scarring and there is no disturbance of the limbal blood-vessels. In this case also the eyes were closed for four days and the patient was off work for three weeks.

GROUP 2.—MILD CASES. CONJUNCTIVA HYPERÆMIC AND CORNEAL EPITHELIUM INJURED

Nine cases fell into this group. The earliest seen was three days after the injury, which was caused by vapour. The first thing noticed was a feeling of soreness in the eyes and throat on waking in the night nine hours after exposure. The left eye was slightly worse than the right. The voice was hoarse. The eyes could be opened but there was photophobia and lacrimation (which were still present at examination). The conjunctivæ were hyperæmic and the corneal epithelium in the palpebral aperture was œdematous (epithelial bedewing) and faintly grey and slightly hazy. In the left eye a few minute punctate staining areas could be seen in the œdematous area. (In one case this was still visible at

nine days.) In the right eye a few fine, shining lines could be seen in the centre of Descemet's endothelium and the outer side of the iris was hyperæmic. This seemed to show that there was some penetration deep to the epithelium, but there was no œdema of the substantia propria and the condition cleared up completely in both eyes. Three months later both corneæ were normal, with slight conjunctival hyperæmia. The triangular white patches of cónjunctiva often described at the limbus are not seen in either Group 1 or 2. They occur only in more severe lesions. The lesion in this patient resembles very mild epithelial damage in the rabbit.

The epithelial bedewing subsides, but before complete restoration to normal there is a stage at which a linear group of isolated shining dots (single hydropic epithelial cells) can be seen with the slit-lamp in the line of the palpebral aperture. In mild cases this is all that may be seen by the fourth day. In slightly more severe cases they may remain visible for from four to six weeks. These may be present even in patients who have not made much complaint. In one case in which the eyes were completely closed for one day the patient was able to return to work in forty-eight hours (though the lids were sore for three days more), but hydropic cells were present in fairly large numbers for three weeks and could just be detected for six weeks.

One case in this group was unable to open the eyes for four to five days, one for one day, while the rest stated that though the lids were swollen the eyes could just be opened.

GROUP 3.—SEVERE CASES. CORNEAL EPITHELIUM AND SUBSTANTIA PROPRIA ŒDEMATOUS. INVOLVEMENT OF CONJUNCTIVAL VESSELS, ESPECIALLY THE LIMBAL SUPPLY

Four cases fell into this group, of varying degrees of severity. In these cases and in those of Group 4 we begin to be able to draw a definite parallel between the lesion in man and in rabbits, since in none of the rabbits was the lesion slight enough to produce Group 1 alone and seldom Group 2.

The first case had had fairly severe exposure to vapour in the laboratory, having worked unprotected in it for some hours as he had a cold and could not smell it. He noticed irritation that night and by 7.30 a.m. was sure he had been burnt. He was admitted to hospital by 2 p.m. in very acute pain, with the lids swollen, eyes closed, chest affected, hoarse voice and burns on hands and arms. Phenolaine was dropped into the eyes with no effect. He was then given atropine and cocaine with considerable relief. The lower part of both corneæ was hazy and swollen. There was definite œdema of the substantia propria. In the left eye there were subconjunctival hæmorrhages at the limbus below and an avascular white necrotic patch in the conjunctiva near the limbus somewhat like the triangular white areas at the limbus described in acute cases in the last war. This condition was still present at the end of a week when I saw him first, but the œdema (primary œdema) of the substantia propria was subsiding fairly rapidly.

The second case was similar and not so severe, though the chest was also affected. I did not see him till three weeks after the accident, when the right eye showed epithelial bedewing only. The left eye (Coloured Plate, fig. 1) showed a small patch of hyperæmia on the palpebral conjunctiva of the upper lid, a slight corneal haze in the palpebral aperture and at the inner canthus a pale triangular area in the limbal conjunctiva. Three months later the corneæ were normal, the granulating area on the lid showed as a healed but intensely red spot, and in the pale area against the limbus the limbal loops were absent, and the vessels beside it slightly hyperæmic. There were no symptoms.

The third case was seen eighteen months after the injury. There were no symptoms. The corneæ were normal, but in both eyes there were faint, pale, triangular areas at the limbus (their apices pointing to the inner and outer canthi) in which the limbal capillaries were absent and their place taken by a sparse and irregular arrangement of larger vessels. This appearance is sometimes called "marbling".

The fourth case, which was first seen a week after the injury, has been watched for over three months and promises to be the most severe and also the most instructive, since the period for which we have no accurate records even from the last war is that from three or four months to five or six years after injury.

This man was opening a cock and got a spray of liquid mustard over his face. He was wearing celluloid eye shields. He received first-aid treatment within ten minutes, con-

sisting of washing his skin and eyes with bicarbonate of soda lotion (no copious irrigation of the eyes was given) immediately after which liquid paraffin was dropped into the eyes. In five hours the eyes and lids began to burn. Three hours after this, at eight hours, he was admitted to hospital with both lids extremely swollen and the eyes quite closed. The conjunctivæ were œdematous and the left was even then obviously worse than the right. In three days the lids could just be opened but the sight was misty in both eyes according to the patient. There was no blistering of the lids and no purulent discharge, only clear tears. Cocaine 2% was given whenever pain became excessive and gave great relief. It did not appear to have any harmful action. The right eye improved quicker than the left.

I saw the patient *on the eighth day*.

The right eye was open though the lids were swollen and the conjunctiva hyperæmic. There was no stain. There was diffuse epithelial bedewing across the lower part of the cornea with scattered minute white dots, probably single, hydropic, epithelial cells. The limbal blood-vessels were engorged especially below. The endothelium was normal. This lesion belongs to Group 2 and when seen at three weeks was still hyperæmic. At six weeks it was completely normal again.

The left eye on the eighth day was extremely hyperæmic and the conjunctiva in the palpebral aperture and also to a slighter extent in the fornices was œdematous, gelatinous looking and slightly raised up so that it formed a rim round the cornea which appeared depressed below its level. The vessels were violently congested and towards the outer canthus showed some irregularity of calibre. There was punctate staining of the cornea which was greyish and hazy especially in its central and lower part, presenting the characteristic peau d'orange appearance of the early severe lesion in man. The corneal epithelium was œdematous, the underlying substantia propria showed an altered, more shiny and brighter zone in its anterior one-third (early œdema) with endothelial disturbance and ruckling of Descemet's membrane (fig. 12, Plate V). As the iris was brown, hyperæmia could not be made out. At the limbus on either side in the palpebral aperture were several somewhat circular opaque whitish patches, looking a little like small ulcers or sloughs but not staining with fluorescein. They occupied the position of the triangular patches usually described but were different in shape and extended on to the cornea. They probably correspond to the pale area at the limbus in the sector of application in the rabbit experiment. Their appearance thus suggested those seen in rabbits with a lesion involving corneoscleral junction and lids, at twenty-four hours. This is to be expected if ten days for a man is roughly equivalent to one day for a rabbit.

I next saw the patient at three weeks. He was unable to work. The right eye had recovered except for hyperæmia but he stated that the left had at first improved greatly (probably corresponding to the healing of the epithelium and subsidence of primary œdema) and five days before had relapsed and he now wanted to keep it shut as there was a feeling of a foreign body all the time, especially under the upper lid.

The conjunctiva was not so swollen but conspicuous changes had occurred in it (Coloured Plate, fig. 2). The opaque areas in the limbal region were now present as areas of disturbance and partial destruction of the limbal capillaries. Above and below them were large subconjunctival hæmorrhages and amongst these were many dilated vessels with thromboses.

The cornea was clearer but was covered with a very large number of minute whitish specks, probably closely set hydropic cells (many of them less shiny and whiter than in the milder cases). In the lower part of the cornea there was œdema of the substantia propria, with engorgement of the limbal blood-vessels. With the slit-lamp it could be seen that the texture of the substantia propria was altered in its superficial layers (fig. 13, Plate V). On everting the upper lid an oval patch could be seen on the tarsal plate, white, opaque, with no visible blood-vessels and resembling an infarct. A similar patch was present at the limbus on the inner side. Both were surrounded by engorged vessels. They were similar to conjunctival and lid lesions in rabbits.

I next saw the patient at five and a half weeks. He was unable to work and still had the feeling of a foreign body under the upper lid in the region of the necrotic patch,

which remained dead white. The white patch on the ocular conjunctiva was surrounded by hæmorrhages and extended on to the palpebral conjunctiva below (Coloured Plate, fig. 3). The cornea was much clearer. The œdema of the substantia propria had subsided, though there was still bedewing of the epithelium. The stroma showed an altered texture, best described as a faint dappling, in its superficial layers (figs. 14 and 15, Plate V).

This eye appears to be in the condition of a rabbit at four to five days, when the primary œdema is subsiding, the thromboses and hæmorrhages are still present at the limbus, no vessels having yet grown in, and the eye is rapidly quietening. The dappled appearance in man seems to correspond with the silky change in rabbits. The difference is probably due to anatomical differences in arrangement of cells and fibrils.

At *eight weeks* the patient was back at work, and felt much better. The white patch under the upper lid was smaller and was partially vascularized. Although the man complained of very little the eye appeared rather worse. There was intense engorgement of the ocular conjunctiva around and in the previously seen white patch below and also to the inner side. There was a reappearance of the corneal œdema below and the limbal blood-vessels on either side of the necrotic area were beginning to invade the cornea. There were thromboses at their growing tips and intracorneal hæmorrhages in the superficial layers of the substantia propria (Coloured Plate, fig. 4). The secondary œdema and vascularization were beginning and the condition corresponded to the rabbit at five to seven days. The patient was next seen *seven months* after the injury. He stated that he had recovered and worked until two weeks previously. At that time the feeling of a "lump under the lid" returned. He was off work. He showed minute hæmorrhages around the necrotic patch under the upper lid. The necrotic patch was completely revascularized and contained globules suggestive of fat. There was also some granulation tissue around it. The cornea was still bedewed and in the area of limbal involvement there were some new hæmorrhages from the extending capillary loops in the cornea and also deep in the conjunctiva (Coloured Plate, fig. 4). This case therefore would appear to be in the stage of recurrent hæmorrhages and probable thrombosis which begins in the rabbit after the first month. This history brings out very well the extreme slowness of the changes in man and the likelihood of mistaking a clinical cure for a true cure since a good deal of the process in the more serious lesions is practically symptomless.

Cases such as this in which vascularization and secondary œdema occur may subside and give rise to no further symptoms (cf. the subsidence in rabbits after one to four months). Three such cases from the last war were examined and although they considered that their eyes had recovered completely they all showed typical changes.

The mildest case seen was gassed in 1917 and recovered after six months. One eye remained symptomless, but the other has had severe ulceration following an injury with sand in 1934. The uninjured eye showed destruction of limbal loops and a few varicosities of the conjunctival vessels in the palpebral aperture. The cornea showed epithelial bedewing, a faint dappling in the superficial layers of the substantia propria, and a disturbance of the endothelium (fig. 16*a* and *b*, Plate V).

Two other cases of greater severity but also symptomless were seen. They both showed destruction of limbal capillaries in the white triangular area, varicosities of conjunctival vessels, epithelial bedewing, shiny dots and lines in the substantia propria (fig. 17, Plate V) and also a peculiar appearance, probably diagnostic when it occurs and not so far seen in rabbits. This is usually referred to clinically as "black lines" or "tubes" (fig. 18, Plate V). It is an appearance of branching clefts or spaces running through the substantia propria at all depths and more or less perpendicular to the surface. It does not alter the transparency of the cornea but definitely indicates a deep penetration by mustard gas in the past. It affects only the part of the cornea exposed and not necessarily all of that. It is not present in every case. Sometimes grey lines are seen instead of, or as well as, the "black" clefts. They are not so far explained and probably have no connexion with them. These cases correspond to the healed rabbits with silkiness and the remains of vessels of peculiar shape, examined at nine months.

GROUP 4. VERY SEVERE CASES SHOWING LATE SECONDARY ULCERATION (SO-CALLED DELAYED KERATITIS)

Since we know that the lesion in rabbits continues to show changes for at least nine months or a year and that in the severe cases secondary ulceration (from cholesterin

deposition and fatty degeneration or persistent œdema) may begin in eight to nine months we should expect to find ulceration in man in about eight to ten years when the slow degenerative changes will have reached the requisite stage. The interim period is symptomless since there is no loss of epithelium and the changes are confined to the substantia propria of the scarred area. There is decreasing vascularization as the vessels recede, leaving behind them the deposit of cholesterin, so that clinically the eye appears to be getting better all the time. A study has been made of 39 cases and case-histories of patients at present attending Moorfields Eye Hospital or the Ministry of Pensions for delayed war gas keratitis, and this, together with Mr. T. J. Phillips' examination of 70 cases and my own observations on the course of the recurrent attacks, completes the picture. Coloured Plate, figs. 5 and 6 show a typical case.

Typical Case of Delayed Keratitis

A patient aged 50 was examined. He gave a history of exposure to gas from a gas shell barrage in July 1917. He put on his gas mask, left the lorry he was driving and went into a dugout for some hours. He was in hospital in France for a month and in England for six months during the whole of which time his eyes were kept bandaged. He had burns on the face and his chest was affected. His eyes gradually recovered except for slight dislike of strong light, but his chest has given trouble ever since.

In 1927 he attended an eye hospital for corneal ulceration, especially in the right eye. The individual ulcers healed quickly, often in a few days, but the irregularity of the surface of the cornea increased after each attack (cf. depressed area in rabbit's eye where cholesterin has been cast off, fig. 9, Plate IV) as there seems to be actual loss of substance when the degenerated area ulcerates. His sight therefore steadily deteriorated and in 1931 he was awarded a pension for his eyes. The recurrent ulceration continued and this year he was seen by Mr. Phillips and fitted with Dallos contact lenses. His visual acuity is R. eye = $\frac{6}{36}$, L. eye = $\frac{6}{9}$ not improved by spectacles. With contact lenses which are well tolerated he is improved to R. eye = $\frac{6}{6}$ partly, L. eye = $\frac{6}{5}$, and so far has had no recurrence of ulceration. He shows in the right eye (which has had most ulcers) cholesterin crystals, fatty degeneration, silkiness (seen partly as dappling and partly as fine short lines, slightly different in texture from that in the rabbit, and probably depending on the slightly different shape and size of the cells and fibres in man) and irregular vessels in process of disappearing together with deposition of cholesterin (cf. rabbit, eight months or more). In the left there is less cholesterin, grey and black lines and alteration of the substantia propria.

The astonishing improvement in visual acuity with contact lenses which he shows is seen in all cases and is due to the substitution of the smooth glass for the irregular and uneven corneal surface as the main refracting interface. The good tolerance of all delayed gas keratitis cases for individually fitted contact lenses is associated with a certain amount of corneal anæsthesia from previous destruction of nerve fibres and the effect of the lenses in preventing recurrent ulceration is probably explained by the protection of the partially insensitive cornea from multiple minute injuries. The same beneficial effect is seen from a tarsorrhaphy, but the contact lens has these great advantages, that it is permanent, transparent and improves visual acuity.

All the cases of delayed ulceration (which should not, in my opinion, be called keratitis as it is not an inflammation but a degenerative ulceration) show these changes. The typical picture is of an eye in which the upper part of the cornea and the limbal loops are normal (fig. 19, Plate VI). Across the centre and lower part runs a band of opacity stretching between the white areas on the conjunctiva in which the limbal loops are absent and the few vessels there are, are badly formed. The scar shows great irregularity of surface. At its edges and in its base are cholesterin crystals. It is vascularized by peculiarly contorted and varicose vessels which enter through the normal limbus above and below the worst scars (fig. 20A and B, Plate VI). There may be narrow constrictions, blood islands, intracorneal hæmorrhages and thromboses. The scar shows in addition to the cholesterin, white flocculent masses of fatty degeneration, patches of a fibrillar silky texture and black and grey lines of a peculiar distribution. All these changes except the black lines, have been reproduced in rabbits. The pathology therefore appears as a slow degenerative process. It is initiated by direct chemical action which produces injury and intense œdema. These two factors combined allow invasion of the cornea by newly formed blood-vessels which are extremely abnormal in form. They are derived from both normal and injured conjunctival vessels. As the corneal vessels slowly retrogress in the course of years, blood may be left in the substantia propria. Vascular regression is followed by

cholesterin and fatty degeneration which are responsible, alone or combined, for the "delayed keratitis" (*see* Table II). Although there is said to be a completely quiescent interval of six to sixteen years the eyes show definite diagnostic signs the whole time, and are merely symptomless.

GROUP 5. EXTREMELY SEVERE CASES SHOWING CORNEAL PERFORATION

These cases are very rare in man. I have only seen one which is undoubted and have heard of two others. The patient I examined is now aged 55. He stated that he was in a "pill box" in 1917 and a gas shell entered it and exploded within 6 ft. of him, splashing him with the contained liquid mustard. He felt a splash in his face and eyes. He had a burning sensation for a short time but could open his eyes at once and could see for about ten hours afterwards. Intense discomfort and much swelling of the lids then came on and he was unable to open his eyes for ten weeks. When the lids opened he could at first see practically nothing but in the following nine months his sight improved so that he was able to read with glasses. He worked as a gardener but had frequent attacks of discomfort and burning. For the last fifteen years he has had severe attacks of ulceration and a perforation occurred in the left eye.

At the present time the right eye shows a typical cholesterin scarring which is more severe than usual as the whole cornea is involved and not only the exposed portion. The left eye, however, shows a perforation which has healed with inclusion of iris. This is above the centre of the pupil, is small, almost circular and resembles those seen in rabbits except that it has healed, while in the rabbits complete phthisis bulbi usually resulted. The whole of the rest of the cornea is scarred, vascular and irregular. This patient cannot tolerate contact lenses though they improve his visual acuity from counting fingers to $\frac{5}{60}$ in his better eye.

This case completes the series and corresponds with the rabbits in Group 3. It is probable that only a direct splash in man would cause perforation, though, as we have seen, prolonged exposure to vapour will produce nearly as severe a lesion, the difference between the effects of vapour and the effects of a splash of liquid being merely one of degree and situation. It is thus apparent that the difference between the effects of vapour and the effects of a splash of liquid mustard gas is merely one of degree and situation.

All stages linking the two have been seen and of the severe but symptomless cases described in Group 3 (page 11) one was due to prolonged exposure to vapour in France in the last war and the other to a splash in a laboratory. To-day it is not possible to say which lesion is due to the splash and which to vapour. The vapour burn is, if anything, the worse of the two.

Twenty of the very severe cases from the last war were questioned as to circumstances and length of time in hospital. 15 out of 20 were confined in an enclosed space for some hours in vapour (dugout, trench, cellar, &c.), 8 stated that it was not raining at the time and some gave their opinion that gas was not troublesome during rain. Three were not wearing a gas mask. One wore it all the time, but was several hours in vapour. Ten only wore the mask part of the time. All of them were seriously ill, vomited, and several were unconscious soon after. The average stay in hospital was six months and the average time the eyes were closed was seven weeks. Many stated that their eyes were kept bandaged and this may have lengthened the time. It is probably better not to bandage.

Conclusions

(1) The clinical pathology of the lesion involving the limbus is similar in man and the rabbit (*see* Tables I and II).

(2) The reaction in man and the rabbit is dependent on the size of the dose and the anatomical situation. The effects of vapour and liquid are different only when the actual amount of mustard gas which soaks into the tissues is different, i.e. the difference is quantitative only.

(3) The late keratitis in man is seen as a degenerative ulceration depending on the initial damage sustained by the limbus and cornea, and not on any continued action of mustard gas or any of its breakdown products.

(4) From 3 it follows that in the present state of our knowledge prophylaxis is likely to be much more important than treatment. It is very difficult to assess the value of treatment in man since the dose of mustard gas received can never be known, and no two cases will be comparable. Two eyes of the same patient may be comparable though by no means always, even when the lesions are due to vapour.

TABLE II.—COURSE OF MUSTARD GAS LESIONS IN MAN, COMPILED FROM OBSERVATIONS ON 65 CASES.

Exposure to mustard gas—
no immediate sensation

↓

Burning sensation
Hyperæmia and lacrimation in 2—6 hours

↓

Very mild cases	*Mild cases*	*Severe cases*	
Lids not closed. Conjunctiva hyperæmic. Cornea normal in 24 hours	Injury to epithelium. Punctate staining. Hyperæmia. Œdema of lids and epithelium. *Eyes partially closed*, 3—4 days	Hyperæmia of conjunctiva. *Œdema of epithelium and substantia propria. Damage to limbal blood supply.* Œdema of lids, and eyes closed at 8 hours	*Very severe cases*
↓	↓		
Clears up within a week	Clears up in 4 days to six weeks	Eyes open at 5 days	*Eyes closed* for 7 weeks
	↓	↓	↓
	Healed corneal lesion. *Will not relapse*	Subsidence of primary œdema and beginning *subconjunctival hæmorrhages* 3—5 weeks	*Persistence of œdema*
		↓	↓
		Vascularization and secondary œdema 8 weeks or more	Increased and repeated vascularization. 2 months—1 year
		↓	↓
		Subsidence. *Probably will not relapse*	*Subsidence with vascular scar.* Unsafe. May break down 1—6 years
			↓
			Cholesterin and fatty degeneration
			↓
			Recurrent ulceration 6—20 years
			↓
			Perforation
			↓
			Phthisis bulbi

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PLATE I.

A B

Fig. 1.—A. The dilatations of the smaller radial vessels in one sector of the iris 6·5 minutes after application of liquid mustard gas to the spots indicated in black. B. The same eye at ten minutes. The peripheral vessels are now dilated as well.

Fig. 2.—Appearance of cornea in narrow beam of slit-lamp in the region of two spots of liquid mustard gas (after twenty-four hours). These are shown by darker shading and are thinner than the surrounding paler area which stains more deeply than they do.

Fig. 3.—Appearance of corneal œdema in the narrow beam of the slit-lamp.

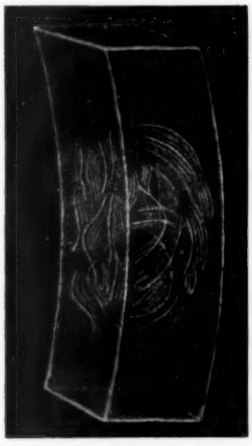

Fig. 4.—Appearance of "silkiness" in the broad beam of the slit-lamp.

PLATE II.

Fig. 5.—Some varieties of pigment slide formed during healing of the sectorial lesion.

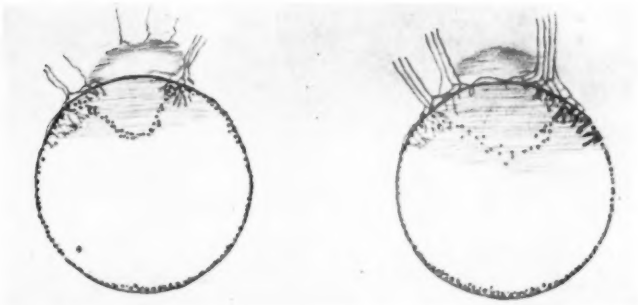

Fig. 6.—Diagram of a cornea showing progress of invading vessels. The injury is a sector in the upper part. The pigment slide is shown and the shaded portion is œdematous. The vessels enter first through the undamaged limbus.

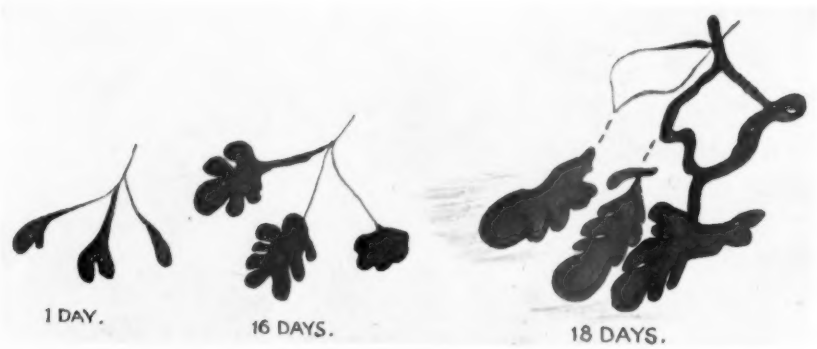

Fig. 8.—The genesis of a group of blood islands, with constriction of their feeding vessels.

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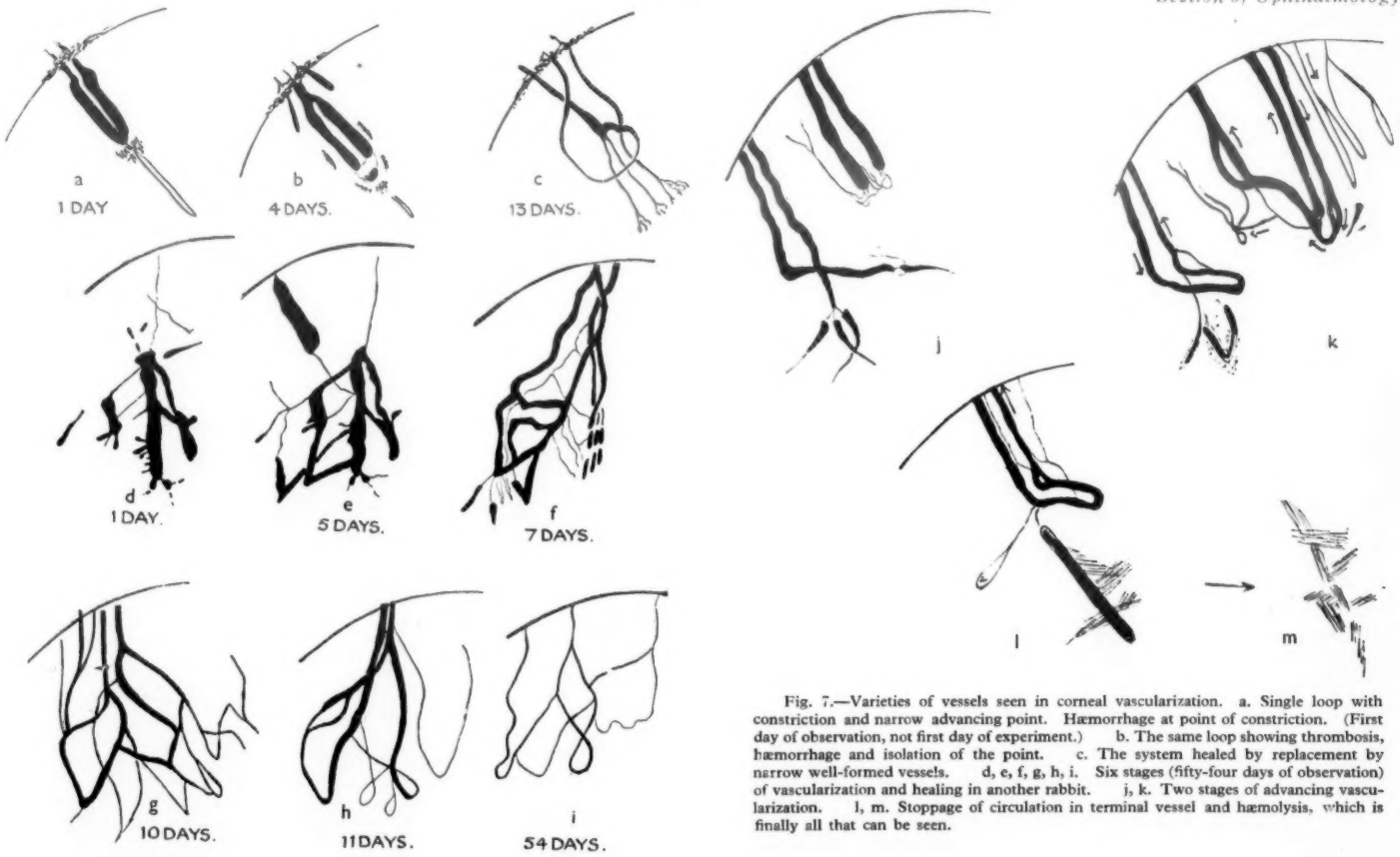

Fig. 7.—Varieties of vessels seen in corneal vascularization. a. Single loop with constriction and narrow advancing point. Hæmorrhage at point of constriction. (First day of observation, not first day of experiment.) b. The same loop showing thrombosis, hæmorrhage and isolation of the point. c. The system healed by replacement by narrow well-formed vessels. d, e, f, g, h, i. Six stages (fifty-four days of observation) of vascularization and healing in another rabbit. j, k. Two stages of advancing vascularization. l, m. Stoppage of circulation in terminal vessel and hæmolysis, which is finally all that can be seen.

PLATE IV.

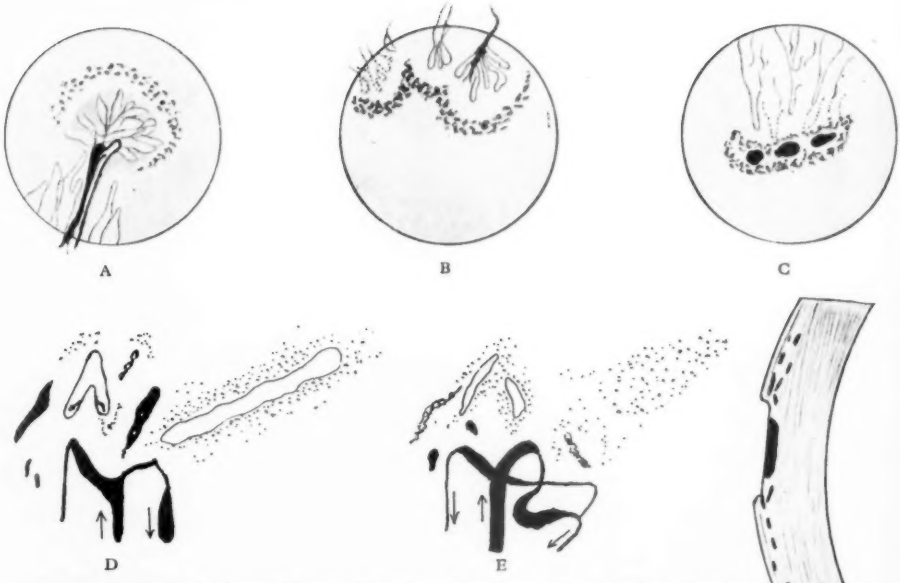

Fig. 9.—Deposition of cholesterin in scars and recurrent ulceration. A. Semicircular cholesterin deposit round arborizing vessel. B. Circinate cholesterin scar. C. Recurrent ulcers. The black spots represent staining areas. D. Empty vessel surrounded by cholesterin crystals, and other detached ends or vessels partly empty. E. Disappearance of many of these. F. Position of cholesterin in C at edge of ulcer seen in narrow beam.

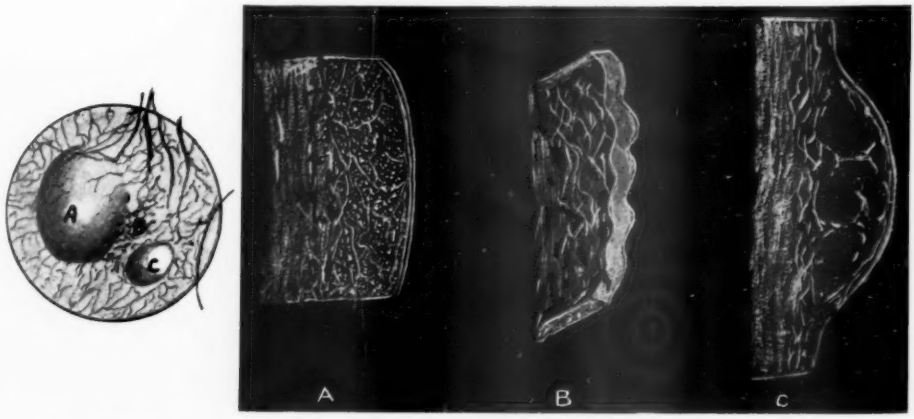

Fig. 10.—Appearance of cornea of badly injured eye. A. Section (narrow beam) through the blister-like protuberance at A. This shows fibrils in a jelly-like matrix filled with minute bright spots, the blood-vessels (black) running deep to this. B. A broader beam section through B, showing formation of fibrous tissue with blood-vessels running among the new fibrils. C. Section (narrow beam) through the bleb at C. The fluid is in spaces in the superficial layers of the stroma and not truly subepithelial. There is granulation tissue in the angles, invading the bleb, which will in time become completely converted into solid vascular connective tissue.

PLATE V.

(I. M., copied by Hamblin.)

Fig. 11.—Two eyes of rabbit with recurrent ulceration from persistent œdema and fibrous tissue formation. The areas surrounded by the dotted lines stain with fluorescein.

Fig. 12.—Appearance of cornea in Case 4 (Group 3) in the narrow beam of slit-lamp at one week. The epithelial surface and œdema of the substantia propria are to the right, the endothelial irregularity to the left.

Fig. 13.—Appearance of cornea in Case 4 (Group 3) in the narrow beam of the slit-lamp at three weeks, showing shiny dots in the substantia propria (cf. fig. 12).

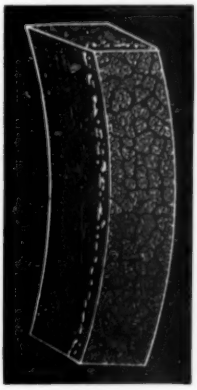

Fig. 14.—Appearance of superficial dappling in Case 4 (Group 3) seen in broad beam at five and a half weeks.

Fig. 15.—Case 4 (Group 3) seen in narrow beam at five and a half weeks.

a

b

Fig. 16.—The mildest Group 3 case. Appearance of dappling and endothelial change seen in *a*, the broad beam, and *b*, the narrow beam of the slit-lamp, twenty-three years after the injury.

Fig. 17. — Shiny dots and lines in the substantia propria many years after exposure.

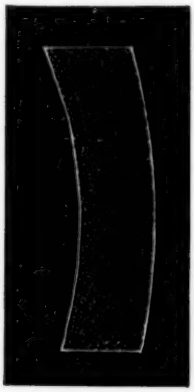

Fig. 18.—"Black-lines" or "tubes" seen in narrow beam of slit-lamp many years after exposure.

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PLATE VI.

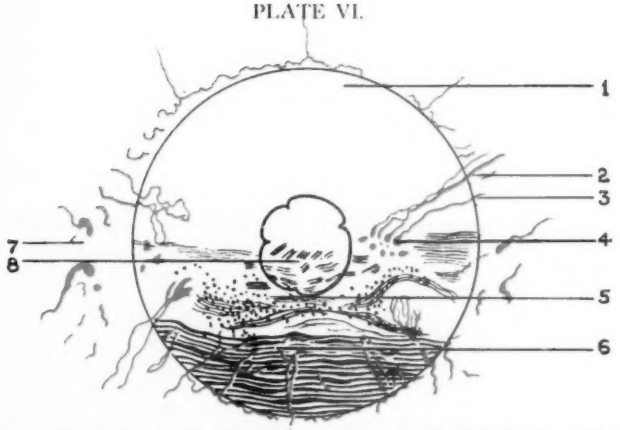

Fig. 19.—Scheme showing characteristics of scar ten to twenty years after severe gassing. 1. Normal cornea and normal limbus, protected by upper lid. 2. Vessels entering cornea from conjunctiva at unscarred limbus and running down to scar. 3. Area of destruction of limbal loops. 4. Vessels in cornea showing thrombosis and hæmorrhages. 5. Cholesterin and fatty degeneration. 6. Depressed scars of late ulcers. 7. Pale area and varicose conjunctival vessels. 8. Outline of pupil showing posterior synechiæ. Fatty degeneration of overlying cornea.

A

Fig. 20.—A. Detail of scar in Group 4 case subject to recurrent ulceration. Note abnormal vessels, cholesterin and fatty degeneration, and silky fibrillar appearance. At (a) the endothelial wall of a disappearing vessel can be seen surrounded by cholesterin. B. Further details of abnormal vessels.

COLOURED PLATE

FIGS. 1 TO 6.

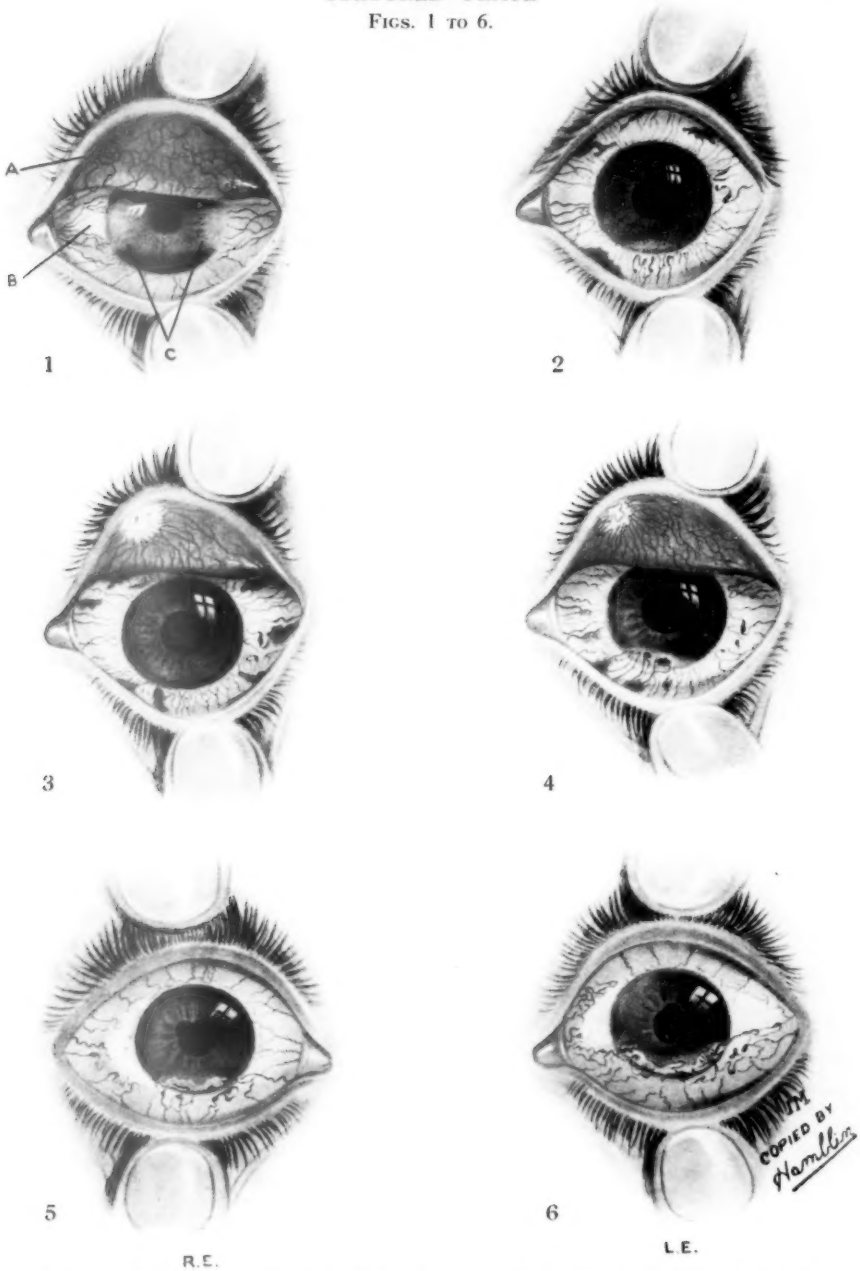

Fig. 1.—Left eye of Case 2 in Group 3. A. Patch of hyperæmia. B. Triangular white patch. C. Corneal haze. Fig. 2.—Left eye of Case 4 in Group 3 seen at three weeks. Fig. 3.—Left eye of Case 4 in Group 3 seen at five and a half weeks. Fig. 4.—Left eye of Case 4 in Group 3 seen at eight weeks. Figs. 5 and 6.—Group 4 case, twenty-three years after exposure to mustard vapour and thirteen years after the first attack of delayed ulceration. R. E. shows plaque of fibrous tissue at limbus on outer side, abnormally arranged and varicose conjunctival vessels and gross scarring of lower part of cornea and limbus. A few posterior synechiæ. L. E. shows triangular pale areas at limbus, abnormal conjunctival vessels, dense corneal scarring and posterior synechiæ. The varicosities are slightly exaggerated in the drawing.

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JOINT DISCUSSION No. 1

Sections of Otology and Laryngology

[*December* 5, 1941]

Chairman—F. W. WATKYN-THOMAS, F.R.C.S.
(President of the Section of Otology)

DISCUSSION ON THE EFFECTS OF FLYING ON THE NOSE AND EAR

A GENERAL SURVEY OF OTORHINOLOGICAL CONSIDERATIONS IN SERVICE AVIATION

Wing Commander J. F. Simpson, *Senior Ear, Nose and Throat Specialist, Royal Air Force:* The first deleterious effect of aviation ever to be recorded was earache, and this was experienced during one of the earliest balloon flights ever made—to be exact, in 1783. To-day the organ which is perhaps most commonly affected by flying is still the ear. The nose, and in particular its accessory sinuses, can also be affected by flight, but less frequently than the ear.

During the last war many of the problems which face us now were well recognized; but advances in aviation and especially in aerial warfare since that time have intensified some, lessened others, and added new ones. These advances are represented by the great increase in the speed and manœuvrability of modern machines, by the greater altitudes now attained, and by the vastly increased duration of operational flying. Much of this improvement has been accomplished at the expense of greater engine power, and therefore greater noise. The noise of modern aircraft, especially multi-engined 'planes is immense and is responsible for the problem of aviation noise deafness. Recognition of its progressive and permanent character has led to investigation into the nature of the noise, into its mode of effect and to measures of protection against it. Group Captain Dickson has been personally responsible for much of this work. The part played by vibration is not fully understood, but no doubt our comrades in the tanks will be able to throw more light on that subject.

Yet another important change in modern Service aviation as contrasted with that of the last war is the greatly extended use and vital importance of all forms of telecommunication. Through wireless telephony and telegraphy 'planes maintain contact with ground stations and with each other, while members of the crew communicate with each other by means of an internal telephone system. The importance of good hearing in flying personnel is obvious, especially when it is remembered that they must be able to hear efficiently in the most difficult circumstances. Messages may be weak from various reasons and external noise excessive. Under such conditions subnormal hearing is likely to lead to a mistake in the reception of a message with possibly disastrous results. It follows that in the selection of aircrew personnel examination of hearing is of the utmost importance. This in itself presents a separate problem.

The usual hearing test used cannot be regarded as being entirely satisfactory and the results are not comparable. The estimation arrived at by the forced whisper test varies greatly, as it is carried out in different rooms where background noises are variable and is conducted by examiners whose forced whispers are of different intensity and tone, and often of accent. Pure tone audiometry is too lengthy for routine purposes, and in any

case does not give any clue to the quickness-of-interpretation factor of hearing. These difficulties have led to an attempt to find a practical but accurate, rapid and comparable method for grading the ability to hear speech. Squadron Leader Fry, from the Department of Phonetics at University College, London, is now working with us upon this problem.

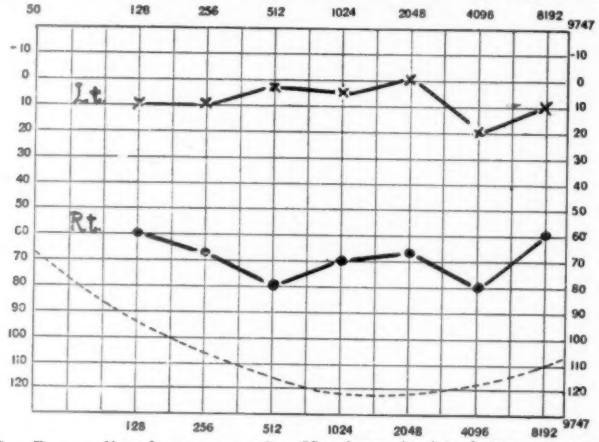
It is by changes in altitude that the commonest and most dramatic disturbances of the ear and nose are brought about. These disturbances depend upon barometric pressure changes and not upon oxygen lack. Until the use of pressure suits or sealed cabins in aircraft is universal the ear and nose will continue to be subjected to pressure changes during climb and descent. With changes of altitude air will flow in or out of the middle ear cleft and sinuses, so that the pressure within them is equalized with that of the external atmosphere. Obstruction to this equalizing mechanism gives rise to one of the commonest and most painful complaints met with in aviation. In the case of the sinuses the pain usually starts in the region of the frontal sinuses, spreads up towards the vertex, radiates between and behind the eyes, and may even involve the upper jaws. The decompression chamber has been largely used in observing this as it is a convenient method of reproducing the effect of large and rapid changes of altitude. I may remark here that no very gross or obvious changes have been seen in the nasal mucosa during these changes of pressure. In the case of the ear, besides pain there is deafness which is often accompanied by certain changes in the drumhead and middle ear, and occasionally though rarely, vertigo. This condition was described in detail by Armstrong in America who called it aero-otitis. Squadron Leader McGibbon will deal with this condition in greater detail.

From a physical point of view the middle-ear cleft and sinuses should be regarded as being essentially the same, both being rigid bony cavities lined by mucous membrane and having small openings to the external air. In the case of the middle-ear cleft, however, there is a small elastic window in one of the walls, the drumhead, and this bulges inwards or outwards according to the difference of pressure on either side of it. Because descent is usually more rapid than climb, and because there appears to be some one-way mechanism that lets air out of more easily than into the middle ear and sinuses, pain is usually, but not invariably, complained of during descent. The pain in the ears and sinuses may be mild, or so severe as to cause an airman to break off a dog-fight and even to make him faint. I have personally suffered such agonizing sinus pain as to drench myself with sweat.

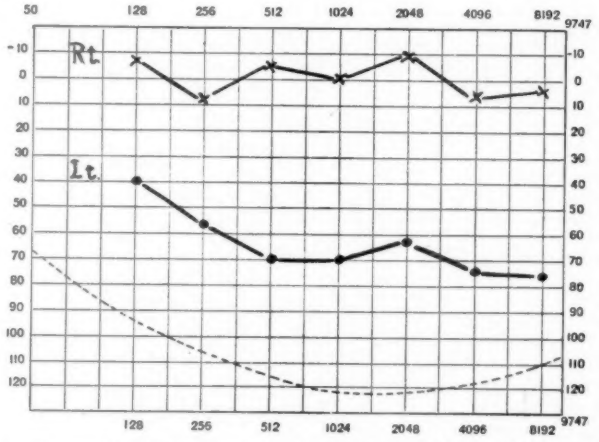
Experiments seem to show that the main factor of the pain in the ear lies not in the bulging of the drumhead, but (as in the case of the sinuses where no drumhead exists) probably in the mucosa or bony walls of the cleft. It is doubtful if the pain can be explained merely on the basis of passive congestion; other and more complex factors probably take part. Congestion can occur as is evidenced by cases of hæmatotympanum and hæmatocele of the antra. A sinister but occasional complication of aero-otitis is a severe and permanent form of deafness. When seen after an interval of some days these cases show no abnormal otoscopic appearances and the Eustachian tubes are clinically patent, but a high degree of deafness which is of the classical "nerve or inner ear" type remains, though in the several cases seen the vestibular reactions were not impaired (*see* audiograms).

Besides alteration in altitude the ear is affected by changes in speed, direction and position in aviation. During the last war much attention was paid to the vestibular reactions towards these changes, especially by Mr. Sydney Scott in this country. It was realized how important a part vision played in correcting the false and illusionary impressions derived from the labyrinth during flight. Without adequate visual reference to the earth or instruments a pilot eventually and inevitably goes into circular motion, develops vertigo, goes into a spin and crashes. The development of the technique of blind flying has overcome this. Essentially this consists in replacing the unreliable vestibular and other sensations by the reading of unfailing instruments which record speed, height, direction, climb, turn and bank. For success the blind flyer must have complete faith in his instruments and must disregard his own sensations. This, however, does not deny the existence of what is termed "flying sense", which is acquired by the experienced pilot who feels himself to be a part of the aeroplane. This "flying sense" will not suffice for blind flying, but is necessary for aerobatics and landing, and amongst other things involves the use of the labyrinth. True pathology of the labyrinth does

Audiograms of Two Cases of Permanent Deafness (Inner Ear Type) following Aero-otitis.



CASE I.—Power dive from 14,000 ft. Has been deaf in left ear ever since. No real pain during the dive.



CASE II.—Power dive from 30,000 ft. to 10,000 ft. Both ears became deafened, the left one recovered in twenty-four hours, but the right one has remained deaf. No pain experienced during the dive.

Both cases had normal tympanic membranes when seen some weeks after the onset of deafness caused by rapid descent. The tympanic membranes bulged on Valsalva's test. The Rinne test was positive and the Weber test lateralized to the unaffected ear in both cases.

not form a practical issue in aviation. The uncontrolled and widespread responses of a somewhat hypersensitive labyrinth are not considered evidence of disease. In practice the routine rotation test has been found to give little reliable help in the discrimination between men who will or will not develop intractable air-sickness and has been given up. Squadron Leader Winfield will be speaking about the problem of air-sickness.

Disease of the ear, nose and throat will impair the efficiency of an aviator, especially under conditions of modern aerial warfare, usually by deafness or by predisposition to

pain. The importance of such affections must be assessed from a Service point of view, which will include that of the Administration and the Treasury. Due allowance must always be made for a generous margin of safety and for the possibility of recurrences. Different views may be taken of the same disability according to whether it occurs in personnel undergoing training, or experienced aircrew. Active suppuration of the ear is, on general lines, regarded as a contra-indication to flying, especially operational flying, if only from the point of view that hearing is affected and quite apart from the fact that treatment is required. It is realized that a suppurating and deaf ear will not actually render a man incapable of flying a machine, but he cannot be considered 100% efficient. This leads to the difficult question of the assessment of a monaural hearing defect as compared with a binaural one. It hinges upon the amount of hearing present in either ear and upon the margin of safety required for the particular duty to be performed.

On similar lines a dry perforation usually means deficient hearing and a chance of recurrence of otorrhœa under Service conditions, but experienced airmen so affected are sometimes used in non-operational work. Provided there is no appreciable hearing loss and that the Eustachian tube is easily opened, a moderate degree of scarring of the drum does not debar from flying, though it is possible that one adherent to the inner wall might give rise to discomfort. Any evidence of past suppuration in the middle-ear cleft should make one suspect that the Eustachian tube might be left with some residual impairment of function. This is shown by the fairly high incidence of cases which give a past history of otitis media amongst those who suffer from aero-otitis. Judging the ease with which a Eustachian tube can be opened is not as simple as one might believe, but it is desirable when examining candidates to have some measurement of this potential patency. Various methods have been employed but it is not unlikely that the only reliable one will involve the routine use of the compression chamber.

All acute inflammatory conditions of the nose and throat are of the greatest importance, as they can interfere with the mechanism for adjusting pressure in the ear and sinuses. For this reason flying with a sore throat or cold in the head is forbidden. Chronic infections are for the same reasons regarded seriously. In this instance, however, the effect is less easy to forecast. We have seen some cases of longstanding sinus suppuration fly and not complain of discomfort. Probably a chronic post-nasal catarrh, associated with a mild and recurrent aero-otitis is as difficult to manage and to legislate for as any case one is likely to meet. Polypi sometimes occur, and in one or two cases of experienced personnel a radical external ethmoidectomy has been followed by absence of symptoms on resumption of flying. The septum is not operated upon unless very definite obstruction and discomfort is complained of. It is not certain that high deviations of the septum have much effect upon the incidence of sinus pain, but it cannot be denied that a submucous resection operation appears to have resulted in the relief of this in a number of cases. Epistaxis, an unpleasant occurrence when the airman is wearing an oxygen mask, is not often met with, but when present the usual leash of vessels in the "bleeding area" is always seen.

My general impression is that considering the number of men flying and the strain imposed upon them, it is remarkable that we do not meet with more aural and nasal disturbances, but this may be due to the careful selection of flying personnel.

AVIATION NOISE DEAFNESS AND ITS PREVENTION

Group Captain E. D. D. Dickson, *Consultant in Otorhinolaryngology, Royal Air Force*: Noise is one of the features of uncontrolled development in a mechanical age —an undesired by-product of the machines which are employed for industrial and war operations. Noise as it affects Air Force personnel arises from the engine and propellers used in modern aircraft. The ill-effects of it have become apparent since the introduction of enclosed cockpits in multi-engined aircraft and the discarding whenever possible by pilots and crews of the flying helmet. In some instances resort has been made to various forms of ear plugs, but these either on account of construction or unsuitability cause discomfort and/or fail to afford the required protection.

Since the introduction of audiometry, studies made by different observers have helped to crystallize the clinical entity of acoustic trauma. Many types of sound stimuli are

known to be injurious to the ear, but my interest has been mainly confined to those arising from exposure to aeroplane noise. The intensity level of such noises is in the region of 120-130 phons. In connexion with flying it arises chiefly from three sources, namely, the engine, the propeller (mainly from the tips of the blades where the velocity is greatest) and the wind (slipstream).

Observations extending over a prolonged period have shown that in a healthy person without history or evidence of aural disease and whose history does not suggest damage by drugs or severe constitutional disease or familial deafness but reveals exposure to noise of an intensity such as I mentioned, a high tone loss must be suspected to represent the effects of acoustic trauma.

It is now generally accepted that the first evidence of such trauma manifests itself as a dip localized to 4,096 cycles per second both for air and bone conduction without involvement of frequency below or above this level, when a 6A Western Electric Audiometer is used. This drop may be restricted at first for some time at this frequency, but repeated and continuous exposure to noise may involve frequencies below this level. The individual may be unaware of any auditory defect and probably notices no disability so long as this loss is restricted to 4,096 cycles per second and is not very marked. Involvement, however, of lower frequencies such as 2,048 or 1,024 cycles per second will constitute a definite impairment of hearing. Results of hearing tests for speech confirm audiometric findings. Mistakes in hearing the spoken word often occur when accurate interpretation depends upon the ability to recognize consonants whose essential characteristics are highness in frequency and weakness in intensity. For example with a 50-60 decibel loss at 4,096 cycles per second, the candidate has difficulty in hearing words like sister, solicitor, &c., from a distance of 20 ft. with a forced whisper whereas he can hear low-pitched words quite easily.

The factors which influence the degree of hearing loss from acoustic trauma are:

(1) The total time of exposure. Individual ears respond in different ways. I have seen a dip at 4,096 cycles after one hundred hours' exposure to aeroplane noise and again have seen only a slight localized drop after exposure for some years.

(2) The length of exposure at each period. The ears can recover with a rest at first but become permanently damaged if exposure continues.

(3) Loud sounds only cause damage.

(4) The character of the sound stimulus, whether continuous or interrupted.

(5) The type of protection adopted.

(6) The surroundings, whether in enclosed or open spaces. A smooth concrete wall will reflect 96% of the acoustic energy striking it.

(7) Previous disease. Previously damaged ears are more susceptible to acoustic trauma than normal ones.

The relation of the frequency to the resultant trauma is not clearly understood. Exposure of the ear to noise of pure tones of 512, 1,024, 2,048, 4,096 cycles per second show a maximum dip an octave above the frequency of the fatiguing note and not at the frequency of the fatiguing note. The common threshold curve with a 4,096 dip was not obtained for a series of tones of an approximate uniform intensity used to produce acoustic trauma. Subjects exposed to a fatiguing note of 2,048 cycles per second showed a localized dip at 4,096. Sounds of low frequency (64-256) produce less acoustic trauma, and certainly no dip at 4,096, than those of high frequency and of approximately equal intensity.

On the other hand analysis of aeroplane noise by means at our disposal has shown that the frequencies of the highest intensity 110-115 db. are at the low end of the acoustic spectrum. Thus it would suggest that a low tone was causing a high tone deafness. Explanation is not clear and I believe that when dealing with a complex noise of high overall intensity, damage is inflicted by the excessive sound pressure on the most susceptible part of the cochlea, that is the basal coil. This by virtue of its situation may probably bear the brunt of the insult.

It is also possible that sudden instantaneous peaks of high intensity, which are not recorded by instruments at our disposal, may occur at 2,048 cycles per second at frequent intervals and thus be responsible for the dip at 4,096 cycles per second. Lastly the external auditory meatus which, as Littler has shown, has in its normal condition a characteristic natural period, may act as a resonator intensifying a frequency in a complex sound in the region of 3,000 cycles per second and thus cause a dip at 4,096 cycles per second.

As to the methods of protection so far as flying personnel is concerned in the Royal Air Force, the wearing of a flying helmet with telephones attached affords the fullest protection. Tests have shown that the characteristic dip at 4,096 cycles per second after exposure to noise does not occur. The other appliances such as ear plugs, plasticine, &c., afford a certain amount of protection, but it must be realized that if full protection against the effects of noise is provided by such appliances, intelligibility of speech becomes greatly reduced. They are, therefore, impracticable from the flying point of view where the use of telecommunication becomes necessary. It is comparatively easy by such means to reduce or damp down the high-pitched tones, and if as recent experiments have demonstrated, high notes of high intensity cause more damage than low ones of the same intensity this may explain the success obtained in protecting ears against the injurious effects of noise by the wearing of a helmet with telephones attached.

A SUGGESTION FOR A NEW METHOD OF TESTING HEARING IN AVIATION CANDIDATES

Squadron Leader D. B. Fry: It is generally agreed that the hearing test at present in use for the selection of flying personnel is not a very satisfactory one, since it fails in some cases to achieve its object. This object is twofold, first, to select for flying duties candidates who will be worth training, for the Service naturally does not wish to train people who will prove eventually unfitted for their duties, and secondly, to ensure that no candidate is rejected who would in fact be capable of carrying out flying duties. Thus the test required to replace the present one is a functional test which will indicate the suitability of a candidate for the duties which he is to undertake.

In the Service hearing is most important from the point of view of signals—a man must be able to hear, recognize and interpret auditory signals, whether speech or morse. The problem of testing such ability is rather complex. Hearing acuity is important and where there are gross hearing losses for pure tones one can predict a certain degree of difficulty in understanding speech, but even here reservations have to be made. If the gross hearing loss is in one ear only, it is quite possible for the subject to be as good at recognizing signals as a normal person with no hearing loss. On the other hand, hearing acuity alone is not enough. Ability to interpret signals depends on both hearing and intelligence, i.e. the ability to guess the right answer. Here we have to notice too the great importance of training, for the ability to guess the right answer is very largely the outcome of training. The question is further complicated by the conditions in which the candidate will have to work if accepted. The chief factor here is a noise background for which a level of 120 phons is not uncommon. Hence we have to ensure that a man can receive signals satisfactorily in these conditions.

From the foregoing it is clear that any kind of threshold testing with pure tones, apart from the difficulties attendant upon such testing, will not tell the whole story. We have therefore had recourse to various kinds of articulation testing, i.e. testing the candidate's ability to receive correctly speech sounds, syllables and sentences. We have said that such tests have to be carried out in conditions approximating to those in which the candidate will have to work. One factor in these conditions, the noise background, has been mentioned already. Another very important one is the aid to understanding which will always be provided by the context; in other words, we are really interested in the candidate's ability to understand sentences, not isolated sounds or syllables. Unfortunately, testing by means of sentences is a long business, because one cannot obtain reliable results without using a large number of sentences. It is evident that if one can establish a significant correlation between ability to receive sentences and ability to receive sounds or syllables correctly, one would be justified in adopting the much quicker and more practicable sound or syllable test. Previous work on articulation testing, chiefly by the Bell Telephone Laboratories, has demonstrated significant correlations between sound, syllable and sentence articulation, but since all such work was done in quiet conditions, it has been necessary to discover first whether such correlations are to be expected when working in a noise field. This work is not yet completed, but we can say that there are indications that significant correlations will appear and it seems probable that the form of test which will be eventually decided upon will be a sound articulation test.

The technique of testing which has been used in the experimental stages is briefly as follows: The subject is placed in a high-level noise field from which his ears are protected by the standard Service flying helmet. The articulation tests, i.e. lists of words and sentences, are then conveyed to him through a pair of telephone receivers carried

in his helmet. It seems unlikely that such a technique will in the end prove practicable for use at all Service medical boards and an alternative one is being developed in which both the background noise and the speech signals are delivered into the candidate's telephones. This is most easily effected by making gramophone records in which the test words or sentences are spoken against a noise background. When this is done it is possible to vary the relative levels of speech and noise, i.e. to change the signal to noise ratio, and to work rather on the principle of the gramophone audiometer. One advantage of using gramophone records and of testing against a noise background is that the acoustic conditions for testing can be reasonably standardized, and a further advantage of this technique is that a number of candidates can be examined at the same time.

The above is a brief indication of the nature of the work which is being done. A great many questions concerning the functional aspect of hearing remain to be answered, and in conclusion I should like to mention one or two of those which are directly connected with the problem of signals.

(1) The importance of training in the reception of transmitted speech. How far can training compensate for defects of hearing (as shown by pure-tone audiometry)?

(2) How much more difficult is it to train a person with defective hearing than one with normal hearing?

(3) What is the effect of monaural deafness on the ability to receive signals? How far is it justifiable to employ in duties involving the use of auditory signals a person who has a gross defect in one ear?

(4) What is the effect of frequency and intensity limitations in the transmission system upon the reception of signals by a person with defective hearing?

These are some of the questions to which the answer is urgently needed.

AVIATION PRESSURE DEAFNESS

Squadron Leader J. E. G. McGibbon: In his survey of the aural lesions associated with flying, Wing Commander Simpson mentioned a group of symptoms which sometimes occurs owing to closure of the Eustachian tube during descent in aircraft—a syndrome known in America as "aero-otitis", and which I have called "aviation pressure deafness".

As I am attached to a Royal Air Force General Hospital which serves many Operational Stations I have had the opportunity to examine a relatively large series of patients suffering from this disability.

26·0% of the total number of aircrew personnel referred to the ear, nose and throat department of this hospital have complained of aural symptoms which have arisen during loss of height in aircraft; and for the purposes of the following notes I have reviewed 100 cases.

I propose to deal shortly with:

(1) *The main features of obstruction of the Eustachian tube,* and

(2) *The nature of the obstruction.*

(1) Proof of Eustachian Blockage has been based on:

A. *Presumptive evidence.* B. *Positive evidence.* (i) *Type of deafness.* (ii) *Otoscopic appearances.* (iii) *Impermeability of the tube to air.* (iv) *Impermeability of the tube to the passage of tympanic catheter or sound.* (v) *Impermeability of the tube to radio-opaque fluids.*

A. *Presumptive Evidence*

(i) *Deafness* alone or in association with other symptoms was the most common complaint of these patients, and this is shown in Table I, which is an analysis of their predominant symptoms:

Table I.—Predominant Symptoms of 100 Patients

Deafness alone	31
Deafness and pain	55
Deafness and tinnitus	5
Deafness and vertigo	3
Pain alone	6
	100

It will be seen that *94 patients* complained of *deafness*, and probably had the last six cases been examined sooner after landing a deficiency of hearing would have been found.

I am convinced that some degree of deafness is a constant symptom of the lesion.

In 10 cases the hearing was normal at the time of first examination. In the remainder deafness was present, and this was of the "conductive" type with loss of acuity for low tones; and although some patients could hear a whispered voice at 20 ft. they mostly suffered from some loss of hearing for the forks C and C1, and from 10 to 30 decibels by the audiometer. In three patients only was there any loss for high tones, but not one of the series manifested the severe and permanent "inner-ear" type of deafness mentioned by Wing Commander Simpson.

It is noteworthy also that deafness was usually the last symptom to disappear.

(ii) *Otoscopic appearances* (six hours to seven days after onset).

(*a*) *Normal drumheads* were seen in 26 patients.

(*b*) *Invagination of the tympanic membrane* of a varying degree was the most common finding and this was noted in 47 patients. The appearances of this condition are familiar, but I would call attention to the word "*invagination*" which was used by Mr. Sydney Scott (1919) in his report of similar cases observed during the last war. It is more truly descriptive than "retraction", as the drumhead is *pushed in* by atmospheric pressure around the middle-ear contents. Invagination of the drumhead was always accompanied by some congestion of the region of the handle of the malleus and of the sheaf of vessels which sweep backwards to the posterior malleolar fold. This vascularity varied in intensity and shaded off into the two following changes:

(*c*) *Attic congestion* which was present in six cases, and

(*d*) *Congestion of the entire drumhead*, which was noted in eight patients. These two conditions simulate, and are often mistaken for, acute bacterial otitis media.

(*e*) *Effusion into the tympanum* was seen in six patients at the time of first examination. Two cases were as usually described, in three patients the effusion was confined to the posterior compartment of the middle-ear, and in one there was a localized effusion into Prussak's space. Two other patients developed tympanic effusion after admission to hospital.

(*f*) *Rupture of the drumhead* was present in seven patients. Six of the perforations were secondarily infected and moist when first seen, the remaining one was dry. In three patients the lesion was in the posterior segment and in four it was anterior to the handle of the malleus.

(*g*) *Evidence of old healed middle-ear lesions*—such as atrophic scars, calcareous patches and local or general increased opacity of the tympanic membrane—was present in several patients in addition to the appearances already described, and four patients had submitted to simple mastoidectomy in childhood.

B. *Positive Evidence*

(iii) *Impermeability of the tube to the passage of air. Inflation* or "*forced ventilation*" *of the middle ear*, i.e. *passive opening* of the Eustachian tube, leads to a consideration of the pressures that can be created in the nasopharyngeal and nasal cavities by different procedures.

(*a*) *Valsalva's method of inflation* is the generally accepted proof of tubal patency, and its successful performance is insisted on by the Royal Air Force before acceptance for aircrew duties. 21 patients could inflate their middle ears by this method when first examined. The average pressure found to be necessary to cause air-entry through a *normal* tube was found to be 30 mm.Hg. The average maximum pressure that could be produced by 100 unselected patients was 114 mm.Hg, and the maximum achieved by any one patient was 220 mm.Hg.

(*b*) *Valsalva's method combined with swallowing movements* was successful in one case in which Valsalva's manœuvre alone had failed. It has been difficult to measure the pressure created by this combined procedure but estimations have been carried out in five patients with a perforated drumhead and patent Eustachian tube. The manometer was connected by an accurately fitting nozzle into the external auditory meatus and, whilst the subject maintained a constant pressure by auto-inflation, when he swallowed the mercury rose on an average 20 mm., and then suddenly fell. I think the success of this method was due to two factors:

Increased patency of the tube brought about by swallowing and

A further, though slight, increase of nasopharyngeal pressure caused by the air-content of the pharynx being forced into the nasopharyngeal and nasal cavities during the "closed phase of the pharynx" (Barclay, 1930) whilst the anterior nares were occluded.

(*c*) *With Politzer's bag* the average maximum nasopharyngeal pressure obtained was 210 mm.Hg.

(*d*) *With the Eustachian catheter* in the tubal orifice estimation of the maximum pressure at its tip has been made and found to be 320 mm.Hg. In only one case was inflation by Eustachian catheter successful at the first visit.

(*e*) *Inflation through a tympanic catheter* was successful also in one patient, but the pressure created in the Eustachian tube was not measured.

(iv) *Impermeability of the tube to a tympanic sound and/or catheter.*—An attempt to pass a tympanic sound or catheter was made in 57 patients and *in all* the passage of the instrument was arrested by a firm obstruction at a distance varying from 0·5 cm. to 2 cm. from the tip of the catheter.

(v) *Radiological evidence of obstruction after the injection of radio-opaque fluid* into the Eustachian tube has been demonstrated in 36 patients of this series by Squadron Leader Rees-Jones and myself. The technique and results in 34 of these have been published (1941), but I would mention that in two patients the obstruction was at the isthmus, in one at 0·5 cm. from its pharyngeal orifice, and in the remaining 33 at intermediate situations.

(2) The nature of the tubal obstruction

Commonly the lumen of the posterolateral half of the cartilaginous tube is closed by contact of its mucosal walls and possibly by a film of mucus; but the extent and degree of closure vary individually, and in a small number of people the tube is constantly open throughout its entire length.

The question of obstruction of a *normally closed* tube naturally leads to a consideration of the means whereby its *active opening* and *normal ventilation* of the middle ear are brought about.

The cartilaginous tube is cradled by muscles.

From its hamular process and its anterolateral aspect the greater part of the tensor palati muscle takes origin (fig. 1).

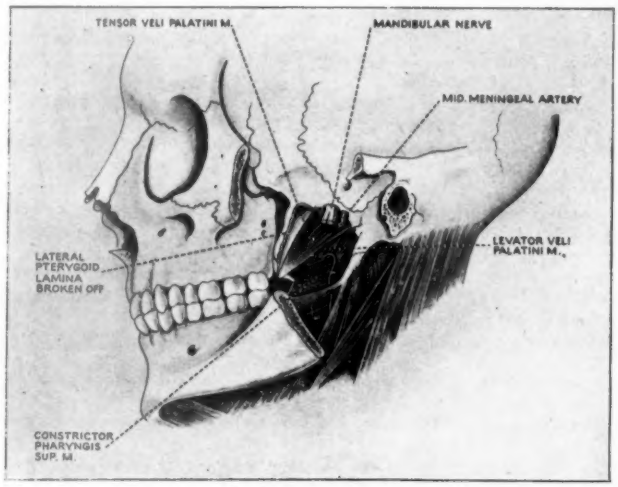


Fig. 1.

Its postero-medial wall is in contact with the levator palati muscle and some of the fibres may arise from this wall. This muscle gradually comes to lie on the inferior aspect of the tube to form the floor of its pharyngeal opening (fig. 2).

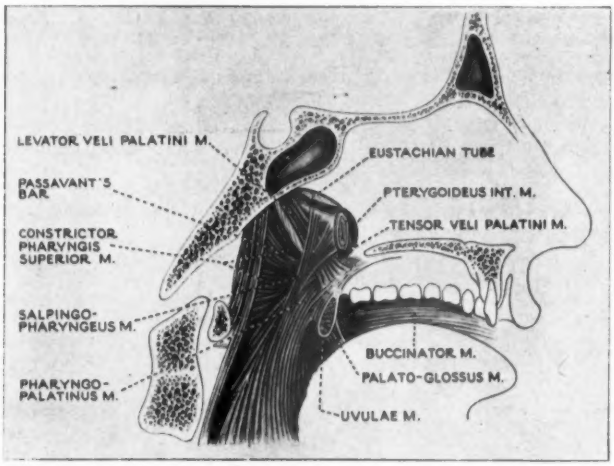


FIG. 2.

The slender salpingo-pharyngeus muscle takes origin from the cartilage near its free extremity, whilst below it is the upper margin of the superior constrictor muscle and that portion of the palato-pharyngeus muscle which forms Passavant's bar (fig. 2).

Functionally the muscles of importance are:

(1) *The tensor palati muscle;*
(2) *The superior constrictor muscle* in its upper part; and
(3) *The sphincter of the pharyngo-nasal isthmus*, which is formed by:
  (*a*) *The soft palate* anteriorly;
  (*b*) *The palato-thyroideus* (posterior pillar) laterally; and
  (*c*) *Passavant's bar* posteriorly.

The mechanism of active opening of the tube has long been controversial, and McMyn (1940) has recently and fully summarized the existing theories. He concluded that the tube is opened by the tensor palati muscle which causes relaxation of its membranous wall, and that other muscles (levator palati, salpingo-pharyngeus, superior constrictor) *may* act synergically.

My own conception is that the tube is opened in a sinuous manner by the combined action of the sphincter of the pharyngo-nasal isthmus and of the upper part of the superior constrictor muscle which drag the postero-medial cartilaginous wall inward: whilst simultaneously the tensor palati muscle braces the antero-lateral wall against the medial pterygoid lamina and draws down the hamular process of the cartilage to relax the membranous wall (fig. 3).

It is known that the tube is opened by swallowing, yawning and gaping movements: that opening may occur during phonation depending on the amount of contraction of the pharyngo-nasal sphincter; and that certain physiological factors such as posture and exercise influence its patency.

Closure of the tube in the majority of individuals is passive and due to the elasticity of the cartilage.

VENTILATION OF THE MIDDLE EAR DURING FLIGHT

During ascent in aircraft or decrease of pressure in a chamber, as the extratympanic pressure becomes less, egress of air from the middle ear along a normal Eustachian tube

is *easy and automatic*. Most aviators are aware of periodic and involuntary escape of air from their Eustachian tubes. This was first described in 1879 (Hartmann) and more recently by Armstrong and Heim (1937). As a result of experiments they state that at 500 ft. (15 mm.Hg) there is a "click" and air escapes from the Eustachian tube leaving a residual positive intratympanic pressure of 3·6 mm.Hg, and that this escape recurs once at an average ascent of 425 ft.

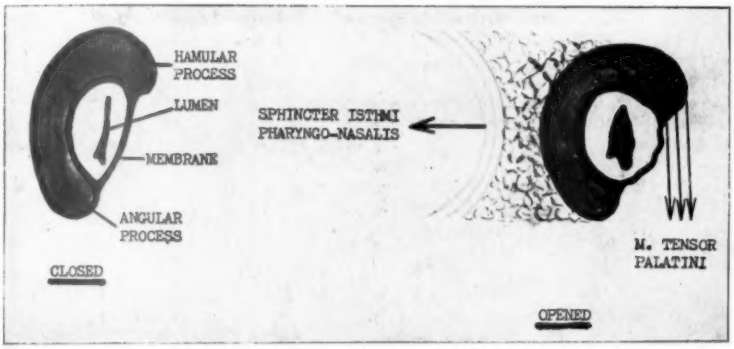


FIG. 3.—Mechanism of tubal opening.

During loss of height in aircraft or increase of pressure in a chamber, the Eustachian tube behaves in an entirely different manner; for, even with a normal tube, air does *not* enter the middle ear automatically. In the majority of aviators, however, the tube is opened and ventilation of the middle ear brought about by involuntary swallowing movements, which occur at the rate of once every sixty to seventy-five seconds in normal individuals; and in addition all aircrew personnel are taught to practise auto-inflation at every 1,000 ft. loss of height.

Non-ventilation of the middle ear during descent results from either:

(1) *Failure to open the tube,* or (2) *Inability to open the tube.*

(1) *Failure to open the tube* may be due to:

(*a*) *Ignorance* as to the correct means to achieve patency.

(*b*) *Lack of opportunity* to open the tube, and this has been responsible when energetic evasive action to escape searchlights or anti-aircraft shells has been necessary. *Rapidity of descent per se* is *not* a *cause of non-ventilation* and is of importance only in this respect. In a large number of patients of this series symptoms became manifest during a *gradual* loss of height from 14,000 ft. or 12,000 ft. when returning from an operational flight.

(2) *Inability to open the tube* owing to the presence of some existing tubal abnormality may have occurred, but in two patients only was œdema of the tubal ostium observed and in one, an old injury of the torus.

Table II is an analysis of the upper respiratory abnormalities noted in the present series.

TABLE II.

EXISTING LESIONS OF UPPER RESPIRATORY TRACT	
"Cold"	6
Deviated nasal septum 18:	
Operation performed	8
Operation not advised	10
Chronic infection of adenoid	2
Chronic tonsillitis	7
Antral infection	10
Dental lesion	1
REMOTE LESIONS OF UPPER RESPIRATORY TRACT	
History of earache and/or otorrhœa	10
History of myringotomy	1
Previous cortical mastoidectomy	4
Previous injury of Eustachian orifice	1

It will be seen that of these—6 patients were suffering from coryza; 8 showed gross septal deformities; 19 had infected tonsils, adenoid or antra; and 1 an old injury—i.e. one-third only of 100 patients were suffering from lesions which *might* have affected the lining of the tube.

If ventilation of the middle ear does not take place *from any cause* during loss of height a positive pressure, depending on the amount of loss and the altitude at which it occurs, develops outside the middle-ear cleft. Armstrong and Heim (1937) have shown that an extratympanic positive pressure of 90 mm.Hg or more will cause the tube to "lock", as the muscles concerned are unable to overcome this force (fig. 4).

When one considers the cartilaginous portion of a Eustachian tube it is realized how easily its cartilaginous and soft membranous walls can be pressed together, completing the impermeability of what is already only a potential lumen.

This occlusion due to pressure I have regarded as *Primary* (*Pressure*) *Occlusion;* and this partially explains the obstruction. If this were all, however, it could be relieved by one

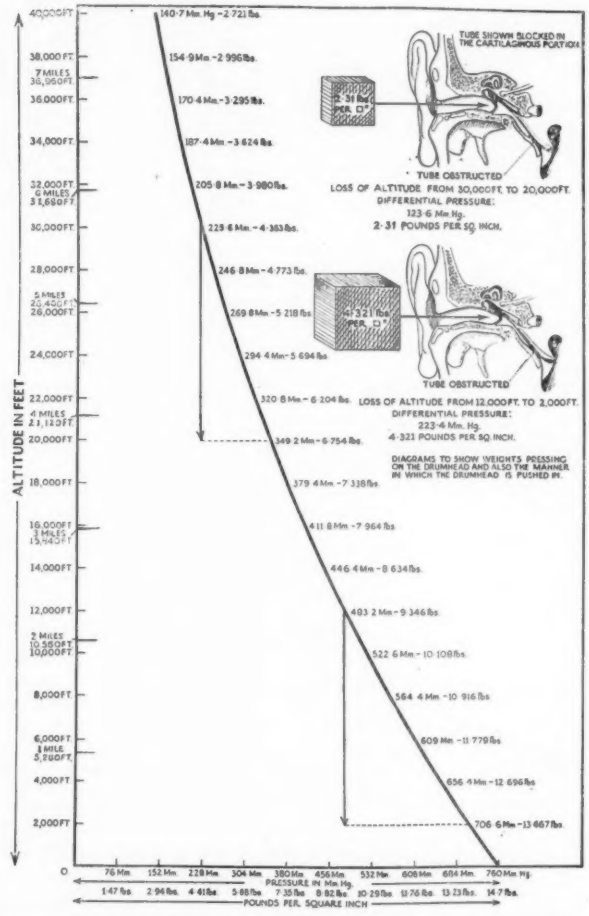

ALTITUDE IN FEET
40,000FT
38,000 FT
7 MILES 36,960FT
36,000FT
34,000FT
32,000FT
6 MILES 31,680FT
30,000FT
28,000FT
5 MILES 26,400FT
26,000FT
24,000FT
22,000FT
4 MILES 21,120FT
20,000FT
18,000FT
16,000FT
3 MILES 15,840FT
14,000FT
12,000FT
2 MILES 10,560FT
10,000FT
8,000FT
6,000FT
1 MILE 5,280FT
4,000FT
2,000FT
0
140·7 Mm. Hg = 2·721 lbs.
154·9 Mm. = 2·996 lbs.
170·4 Mm. = 3·295 lbs.
187·4 Mm. = 3·624 lbs.
205·8 Mm. = 3·980 lbs.
223·6 Mm. = 4·323 lbs.
246·8 Mm. = 4·773 lbs.
269·8 Mm. = 5·218 lbs.
294·4 Mm. = 5·694 lbs.
320·8 Mm. = 6·204 lbs.
349·2 Mm. = 6·754 lbs.
379·4 Mm. = 7·338 lbs.
411·8 Mm. = 7·964 lbs.
446·4 Mm. = 8·634 lbs.
483·2 Mm. = 9·346 lbs.
522·6 Mm. = 10·108 lbs.
564·4 Mm. = 10·916 lbs.
609 Mm. = 11·779 lbs.
656·4 Mm. = 12·696 lbs.
706·6 Mm. = 13·667 lbs.
TUBE SHOWN BLOCKED IN THE CARTILAGINOUS PORTION
2·31 lbs PER □"
TUBE OBSTRUCTED
LOSS OF ALTITUDE FROM 30,000FT. TO 20,000FT.
DIFFERENTIAL PRESSURE:
123·6 Mm Hg.
2·31 POUNDS PER SQ. INCH.
4·321 lbs PER □"
TUBE OBSTRUCTED
LOSS OF ALTITUDE FROM 12,000FT. TO 2,000FT.
DIFFERENTIAL PRESSURE:
223·4 Mm. Hg.
4·321 POUNDS PER SQ. INCH.
DIAGRAMS TO SHOW WEIGHTS PRESSING ON THE DRUMHEAD AND ALSO THE MANNER IN WHICH THE DRUMHEAD IS PUSHED IN.
76 Mm. 152 Mm. 228 Mm. 304 Mm. 380 Mm. 456 Mm. 532 Mm. 608 Mm. 684 Mm. 760 Mm. Hg.
PRESSURE IN Mm. Hg.
1·47 lbs. 2·94 lbs. 4·41 lbs. 5·88 lbs. 7·35 lbs. 8·82 lbs. 10·29 lbs. 11·76 lbs. 13·23 lbs. 14·7 lbs.
POUNDS PER SQUARE INCH

FIG. 4.—To demonstrate the amount of positive extratympanic pressure developed by equal loss of height at different altitudes.

of the recognized forms of inflation, and in many patients such relief has been achieved when the treatment has been applied within a *short time* of the onset of symptoms.

If, however, "forced ventilation" of the middle ear is not available or is neglected for one to two hours, the tube becomes impermeable to air even at high pressures, fluids and sounds as mentioned earlier.

It is reasonable to assume therefore that some biological change has taken place as a result of the primary (pressure) occlusion, and this I have called *Secondary (Vital) Occlusion.*

The nature of these secondary changes is not known but it can be surmised when one views the thickness of the submucosa and the large numbers of mucous glands and goblet cells which are present in the epithelial lining of the cartilaginous tube.

Secondary occlusion is a *very real* entity and it may take as long as fourteen weeks to resolve, as happened in one patient of this series.

The ætiology of this type of aural defect appears to be:

Failure or inability to open the tube → Primary Pressure Occlusion → Secondary vital occlusion

REFERENCES

ARMSTRONG, H. G., and HEIM, J. W. (1937), *J. A. M. A.*, **109**, 417.
BARCLAY, A. E. (1930), *Brit. J. Radiol.*, **3**, 538.
HARTMANN, A. (1879), "Experimentelle Studien über die Funktion der Eustächischen Röhre". Leipzig.
MCMYN, J. R. (1940), *J. Laryng. & Otol.*, **55**, 1.
REES-JONES, G. R., and MCGIBBON, J. E. G. (1941), *Lancet* (ii), 660.
SCOTT, S. (1919), *Spec. Rep. Ser. med. Res. Coun.*, Lond., **37**, 34.

OBSERVATIONS ON AIR-SICKNESS

Squadron Leader R. H. Winfield: The causation of air-sickness may be considered from three points of view—physiological, pathological and psychological, although the condition may be due to any combination of these three factors.

(1) *Physiological*

When one flies for the first time, whether as pilot, observer or passenger, the labyrinth is subjected to a series of new stimuli caused by the unaccustomed motion of the aircraft; in a proportion of subjects the effect of these stimuli is to cause sweating, pallor, nausea and malaise, which may be followed by vomiting. 5 to 10% of those who fly for the first time vomit more than once during their first twelve hours in the air. In the vast majority of cases, however, a physiological adaptation occurs and air-sickness will then only recur if this adaptation is broken; this may be caused by such factors as a spell of prolonged severe aerobatics, a change in the type of aircraft flown, or by an absence from flying for about six months; again just as sea-sickness occurs in very rough weather amongst experienced sailors, air-sickness may occur in experienced personnel when prolonged flights are made in exceptionally bumpy conditions.

The incidence of air-sickness is influenced by what may be called the accessory factors, and the more important of these are:

(1) *The weather.*—Air-sickness is obviously more common in bumpy weather, and in peace-time the pilots of civil aircraft are instructed to fly in strata of calm air in order to prevent air-sickness.

(2) *Type of aircraft.*—Some types of aircraft have the reputation of causing air-sickness more readily than others. Variation of the wing loading is responsible for different types of movement and it is possible that the quick vertical movement associated with low wing loading is a potent factor.

(3) *Noise and vibration.*—The presence of noise and vibration is an important factor, possibly because it predisposes to fatigue.

(4) *Ventilation.*—Aircraft which are not properly ventilated tend to be either draughty or stuffy, while the presence of an oily smell from the engines is conducive to air-sickness.

(5) *Comfort.*—Those travelling by air should be comfortable and not cramped. Room to move about the aircraft and clothing which is warm without constricting are essentials.

(6) *Diet.*—The quantity and quality of food taken before flying and while in the air

must be reasonable; small appetizing meals taken frequently are the most satisfactory.

(7) *Ocular stimuli.*—The unaccustomed disagreement between ocular sensations and those from the labyrinth associated with aircraft movement will cause air-sickness in some subjects. This is well seen in those type of aircraft where the navigator sits at a table and is constantly shifting his gaze from the horizon to his logbook. In bumpy weather he may be subjected to a wave of nausea as he bends his head forward over the table.

Other factors such as cold, anoxia and boredom predispose towards air-sickness.

(2) *Pathological*

The presence of any form of organic disease will increase liability to air-sickness. The more common conditions associated with it are sinusitis and otitis and when these have been cured air-sickness ceases.

(3) *Psychological*

If any of the 5 to 10% of people who have been air-sick during the first twelve hours of flying are subsequently placed in an environment to which they cannot adapt themselves air-sickness may recur as a psychological escape mechanism.

It is interesting to note that when a pilot is flying the aircraft himself he is very rarely sick. This is possibly due to two causes: first, his attention is taken up below the levels of consciousness, and secondly, he is able instantly to counteract the movements of the aircraft by anticipation. That this anticipation of movement is an important factor is well shown by the fact that some pilots will become air-sick when flying with the automatic pilot, which anticipates the aircraft movement for them.

TREATMENT OF AIR-SICKNESS

Drug therapy is limited by the fact that whatever drugs are used cortical function must not be depressed. Treatment, therefore, is directed mainly towards taking care of the accessory factors, which have already been discussed.

The subject must be reasonably fit, adequately fed and suitably clad. He requires protection from noise, and oxygen at oxygen heights. The aircraft must be properly heated, satisfactorily ventilated and made as comfortable as possible.

Section of Dermatology

President—H. C. Semon, M.D.

[*November* 20, 1941]

Case for Diagnosis. ? Seborrheid.—A. C. Roxburgh, M.D.

Mrs. H., aged 51.

History.—Complains that for three weeks she has had an irregular, blotchy, brown staining of the skin of the face, chiefly of the cheeks, which are slightly scaly, and puffiness of the eyelids. Feels tired but otherwise well. She has a history of pyelitis twenty years ago and later subcapsular abscesses of both kidneys and later still a long period of ill-health with streptococcal infections and high temperatures. She has had two miscarriages. She lived in Egypt for two years during the last war but has not lived in the tropics. Her health of recent years has been reasonably good.

Examination.—The brown colour is seen to be due to the presence in the skin of very minute brown semi-translucent nodules most or all of which appear to be follicular. These nodules are seen best on the upper lip where the intervening skin is abnormally white and opaque. On the cheeks the nodules are confluent and the skin is slightly scaly. There is some redness over the ramus of the mandible down on to the neck on each side but the nodules are not easily seen here. The eyelids are only very slightly puffy. The patient has no evidence of rosacea and her head is not scurfy.

I have seen somewhat similar nodules in the past in cases of rosacea and also in one or two young women who had no rosacea. The latter cases I regarded as a form of seborrhœa. These cases cleared up with a few ¼ pastille doses of X-rays and the use of a sulphur and resorcin paste, but I have never been able to ascertain what this condition really is and whether it has been described before. It does not appear to be the "rare seborrheid of the face" described by Pringle (*Brit. J. Derm.*, 1903, **15**, 41) which was a much more papular condition.

Dr. Elizabeth Hunt: I would suggest the possibility of infection by *Microsporon furfur*, although I have never known it affect the face. The brown pigmentation and the scaling are suggestive. Cases of *Microsporon furfur* infection are not often seen nowadays but during the last month I have seen two women with it, both cleanly in their habits. Both had pigmentation of the trunk; one had been referred as a secondary syphilide, the other as an unusual case of Addison's anæmia.

Postscript.—10.2.42: This patient was given four ¼ pastille doses of X-rays and a resorcin and sulphur paste to the face which caused great improvement. Then Dr. Geoffrey Evans prescribed vitamin B_1 and riboflavin. She had two more sixth of a pastille doses of X-rays and then a two weeks' holiday. At the end of this the face was nearly well and the patient's general health very much improved.—A. C. R.

Darier's Centrifugal Migratory Erythema.—A. C. Roxburgh, M.D.

Mrs. B., aged 40. First seen October 1, 1941, when she had a large red area covering the back of the neck with a festooned lower border raised nearly ¼ in. above the surrounding skin and about ½ in. wide. There were smaller similar lesions on the right temple and central forehead. Weekly injections of 10 c.c. of her own blood intramuscularly were advised and of these she had six; by November 12 the lesions had to a large extent involuted but portions of the raised border were still present. On November 12, X-rays (½ pastille) were given to the raised border and the lesions have now entirely flattened out and only the red staining remains. The patient has a seven years' history of attacks of fever of unascertained cause and has been an in-patient for three months, six months and six weeks respectively in three different London hospitals without the cause having been determined. Sulphapyridine controlled the fever but had no effect, she states,

on the erythema. In the past she has had ulcers of the tongue, middle-ear discharge, iritis, glaucoma and cataract of the right eye. Her health is now fairly good apart from the erythema.

The PRESIDENT: In Darier's own description, the lesions have been on the abdomen and flanks in most of the cases. The cause of these peculiar urticarial lesions remains undiscovered.

Severe Chilblains on Right Leg Weakened by Previous Poliomyelitis.—A. C. ROXBURGH, M.D.

Mrs. G., aged 27.

The leg, though weak, is useful and the patient is able to get about easily and play tennis. For the last two to three weeks, since the recent cold spell, she has had a number of cold purple nodules and plaques about 1 inch in diameter on the back and on the lower third of the front of the leg. She states that she has had "ordinary chilblains" before on this leg. She has no chilblains elsewhere. There is no family or personal history of tuberculosis and the lesions seem to be too superficial to be those of Bazin's disease. To-day the lesions have very much improved owing to the warmer weather and are only brownish red in colour. I should be glad of suggestions for treatment, particularly whether any member has experience of bee-venom ointment which was advocated for ordinary chilblains by Watson (*Lancet*, 1941 (i), 301).

Discussion.—Dr. JOHN FRANKLIN: I should be careful about rubbing in bee-venom ointment. I have seen several cases of severe local dermatitis in patients using it for rheumatism. I should be inclined to try galvanic baths, which often help chilblains and should be particularly useful in this type of case.

Dr. F. PARKES WEBER: I suggest that the case is one of the chilblainy type of "erythrocyanosis crurum feminarum frigida", which is always bilateral excepting when one leg is a *situs minoris resistentiæ*. The main treatment in such cases should be preventive by protecting the limb from cold.

Dr. A. C. ROXBURGH: I thank Dr. Franklin for the warning about bee-venom ointment. As to Dr. Parkes Weber's remarks, I should have thought that chilblains of one sort or another on an old "polio" leg were quite common. The patient said they were previously "ordinary chilblains"; that is not my expression.

Acute Lichen Planus.—A. C. ROXBURGH, M.D.

C. L., male, aged 19, sheet metal worker. Acute lichen planus of two weeks' duration, very widespread, confluent over large areas of the trunk and affecting both the penis and the mucous membranes of the cheeks. A big, strong, apparently perfectly healthy youth with no worries. For the last two to three months he has been working twelve hours a day for five days a week and eight hours a day on Saturdays but does not complain of being tired. Can any member report good results from large doses of vitamin B_1 which have been recommended in acute lichen planus?

POSTSCRIPT.—10.2.42: This patient continued at work and was given twice weekly an intramuscular injection of Vitamin B_1 (Benerva 1 c.c.) and took tablets of Benerva 1 mg. thrice daily by mouth. In two weeks the rash was flatter and becoming pigmented, and it has continued to do so till last seen at the end of January. Three or four other patients with fairly acute lichen planus have improved similarly on vitamin B_1.—A. C. R.

Leprosy.—LOUIS FORMAN, M.D.

H. S., male, aged 69.

Lived on the Malabar coast for thirty years. Married, wife and four adult children all well.

Ten years ago he noticed an area of anæsthesia on the right leg, and received treatment for leprosy. Eighteen months ago he developed a general eruption on the face and trunk with fever. When seen a year ago, there was diffuse infiltration of the skin of the face with definite nodules on the forehead and infiltrated plaques and papules on the trunk and limbs. The nasal mucosa was thickened and bacilli were found in the discharge. Save for an absent left plantar reflex and blunting of sensation in the lower leg, there was no abnormality of the nervous system. The nodules on the face were not anæsthetic.

Section from a nodule on the back showed an infiltrate of endothelial cells in the cutis, a sarcoid reaction; leprosy bacilli were scanty.

He was taken into hospital; there was no fever, and now the infiltrations of the face and the nodules on the limbs and trunk have largely subsided, leaving pigmented areas. Since his discharge from hospital he has been giving himself injections of alepol and chaulmoogra oil.

Discussion.—Dr. H. C. STANNUS: The patient was brought to me some time ago to confirm the diagnosis. He is now much better than when I first saw him.

The PRESIDENT: Members should bear in mind that the diagnosis of leprosy must be confirmed by demonstrating the bacillus in the skin. It is not sufficient to take a nasal swab and say the case cannot be one of leprosy because there are no bacilli in the nasal mucosa. In only about one-third of the cases are bacilli recovered from this focus.

Dr. STANNUS: The question of infectivity in leprosy has never been satisfactorily answered. Of course there is danger, but usually the association has to be a fairly close one. In some of the old German leper colonies in Africa to which the leper was allowed to bring his wife and children, the whole family developed leprosy in time. Many of the children did not show signs of leprosy for three or four years, but one can say that eventually they all contracted the disease. Native attendants in the colony gave the treatment. Some of them had been there for many years without developing leprosy. Theirs was a fairly close association but not sufficiently close for them to develop the disease. It was one of the most remarkable sights in these colonies to see a woman with loss of hands and feet due to leprosy nursing a beautiful, fat, perfectly normal newborn baby, and saddening to know that such babies if left in the colony would eventually develop leprosy. Since Great Britain took over the German colonies, families are no longer allowed to go into the leper colony with the affected individual.

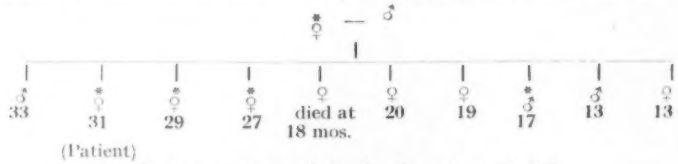
Familial and Congenital Basal-celled Epithelioma in the Distribution of Epithelioma Adenoides Cysticum, and Showing Some of the Histological Changes of the Latter.—LOUIS FORMAN, M.D.

E. S., female, aged 31.

At the age of 15, numerous small nodules appeared around the chin, in the nasolabial folds and in front of the ears, where they are aggregated into small plaques. The nodules are flat or hemispherical and skin-coloured.

Three other siblings and the patient's mother show the same lesions, which appeared at puberty. The two youngest members of the family may develop the disease when they reach puberty.

Section from one of the nodules in front of the ear showed a basal-celled tumour, with cells arranged in columns. One small cyst containing horny material was seen.



Affected members of the family are marked *.

Dermatitis Herpetiformis, with Unusual Limitation of the Disease.—LOUIS FORMAN, M.D.

A. T., female, aged 40.

Thirteen years' history of blisters on the feet and thighs. The blisters ruptured in two days, forming superficial ulcers, and these were diagnosed for a time as artefacts. Three years ago she developed grouped, small, thick-walled blisters on a pigmented patch on the right lower abdomen. There were no eosinophils in the blister fluid and no blood eosinophilia. Potassium iodide gr. v t.d.s. given for a week, provoked erythematous discs on the ankles and knees with numerous thick-walled blisters. 30% iodide ointment applied for five days to the pigmented area on the abdominal wall provoked a fresh crop of blisters.

Sclerodermia with Long Antecedent Pigmentation.—GODFREY BAMBER, M.D.

Miss D. B., aged 20. About thirteen years ago began to get patches of pigmentation which have gradually increased in size and number, and three years ago another kind of lesion began to appear in a pigmented part of the left thigh.

Inspection showed deep pigmentation covering large areas on the lower half of the trunk and smaller patches with indefinite outlines on the upper half and on the proximal parts of the limbs. On the right side of the forehead was another pigmented patch, and examination of the face by Wood's light revealed fairly sharply defined areas of pigment on the other side of the forehead and on the cheeks, a distribution suggesting chloasma.

On the inner side of the left thigh were two nummular patches of sclerodermia, and a fresh area was developing in pigmented skin above the left anterior axillary fold.

Over the upper part of the chest were dilated veins which had been present for years.

General health good. Catamenia regular. B.P. 120/70. No pigmentation of mucous membranes. R.B.C., no abnormality. W.B.C. 7,550, polymorphonuclears 58%, lymphocytes 30%, large monos. 7%, eosinophils 3%, basophils 2%.

Biopsy.—Dr. Freudenthal reported: (*a*) A pigmented area: Except for greatly increased melanin pigment the skin was normal. (*b*) The edge of a sclerodermia lesion: One end of the section showed well-developed sclerodermia with condensed collagen bundles, elastic fibres diminished and partly destroyed, rete pegs flattened. Amount of pigment normal or diminished. The other end showed a great increase in pigment but no obvious signs of sclerodermia.

Discussion.—The PRESIDENT: I have under my care two elderly women with circumscribed sclerodermia, whose lesions are situated in the perineum and, curiously enough, there are two strange atrophic lesions under the clavicle. One of these cases has gone on to almost complete atresia of the vagina.

My intention is to try to relieve the pruritus with thorium X ointment; it is extremely severe and keeps the patient awake.

The atresia above mentioned had been treated by a gynæcologist who did not realize he was dealing with sclerodermia. The stitch wounds took months to heal and the patient was not relieved by the operation.

Acrosclerosis Sellei.—HUGH GORDON, F.R.C.P.

Patient, aged 49, unmarried, telephonist.

History.—Six years ago she complained of pains in the arms, which shot down to the fingers; these became red and inflamed, and small ulcers appeared on the finger-tips, which healed in a few days. The condition was regarded as Raynaud's disease, though no phase of pallor was recorded.

Physiotherapy was carried out for two years with very slight benefit. During the last year her general condition has deteriorated, she has lost weight and has pains in the chest and shortness of breath. The condition of the hands remains unchanged except that they are getting stiffer.

On examination.—She is a wasted woman, with marked wrinkling around the mouth and slightly mask-like facies.

Wasting of the body and the limbs appears to be due to loss of subcutaneous tissue and, possibly, muscle. Except on the hands, there is no suggestion of induration of the skin, which is freely movable and normal to the touch. Pigmentation and telangiectasia were present over the chest and back. The hands were slightly clawlike and hardened. This process was most marked on the terminal phalanges and spread upwards to above the wrist. The hands are bluish in colour and on the tips of all the fingers are stellate scars: the nails are atrophied. X-ray of the hands shows absorption of the terminal phalanges. The mucous membrane of the mouth appears slightly atrophic. General examination is essentially negative. Electrocardiogram normal. X-rays of the chest and heart are within normal limits. W.R. negative. Blood calcium is within normal limits.

The President showed a case in 1936 (*Brit. J. Dermat.*, **48**, 653) as "Acrosclerosis (Sellei) connected with Raynaud's phenomenon". In this case, however, there was no sclerodermic process. I showed a case in 1937 (*Proc. Roy. Soc. Med.*, **31**, 262 (Sect. Derm., 22)) with well-marked sclerodactylia and mask-like appearance with shrinking of the skin around the mouth. I pointed out at that time that the sclerodermic process which was present, appeared to be secondary to a true sclerodermia which had started on the forearms, and had spread down to the hands. In the discussion the general opinion was that Sellei's subdivision could not be substantiated and that cases of sclerodermia were common in which sclerodactylia and shrinkage of the face were well-marked features.

My reasons for putting forward the suggestion that this present case is a true acrosclerosis Sellei (so-called) are: (1) The process started apparently six years ago on both hands and face; in the case of the hands, vasomotor changes were present and pain was

complained of. The face was described as being "tight". (2) Shrinkage had occurred gradually; the clawlike tips of the hands had taken four years to develop; shrinkage of the face had taken place two years ago and of the body one year ago. (3) The hands were now hard to the touch, but there was no true process of sclerodermia present. (4) The appearance of the finger-tips and X-ray changes were as described by Sellei. (5) Telangiectasia and atrophic appearances of the skin were present elsewhere on the body.

Discussion.—Dr. PARKES WEBER: The case is a typical example of what was formerly termed "symmetrical atrophic sclerodermia with sclerodactylia". The muscular atrophy in the hands and the bony absorption in the terminal phalanges has been commonly supposed to be secondary to disuse and pressure from the hide-bound condition of the integument, but there may be other causative factors.

Dr. R. KLABER: I was impressed by the degree of wasting, which seems to involve not only the subcutaneous but also the muscular tissues. Is that degree of wasting a feature of either acrosclerosis as described by Sellei, or of generalized sclerodermia?

Dr. W. FREUDENTHAL: One thinks that sclerodermia might affect the muscle secondarily just by pressure of the skin getting tighter, but it seems also possible that the muscle is primarily involved. The aspect of the question has been widened since dermatomyositis has been included in the sclerodermia group. See papers read by T. Lewis, G. B. Dowling, W. Freudenthal and W. J. Griffiths, *Brit. J. Dermat.*, 1940, **52**, 233, 242, 289 and 296.

The PRESIDENT: I remember reading of a post-mortem on one of the cases in which it was pointed out that not only were the muscles of the skin involved in the sclerodermatous process but also the endocrine glands, particularly the adrenal cortex, so that a general process must be hypothesized.

Dr. FREUDENTHAL: There are not very many cases of generalized sclerodermia on record in which a microscopic post-mortem examination of the endocrine glands has been done. Amongst these, as Dowling has pointed out, the thyroid gland was found to be nearly always involved.

Dr. GORDON: I cannot agree that this patient can be considered as a case of generalized sclerodermia. Her skin is unthickened all over the body. Though the hands are clawlike, this is due to a general process of shrinkage.

The PRESIDENT: I agree. The extremities are picked out in this case.

Ehlers-Danlos Syndrome.—HUGH GORDON, F.R.C.P.

Patient aged 46, single, housemaid.

She attended hospital two months ago with a history of falling in the street and splitting the skin of her right calf. This was said to have bled profusely, though bleeding was not apparent on examination.

The skin tear measured 2 in. and it was noticed that the deep fascia had also split about ½ in. This wound healed by granulation within a month.

She reported that this skin splitting on trivial trauma had been common in the past. Bleeding was often profuse and had on occasions to be controlled by suture. She stated that she had bled profusely from a tonsillectomy and teeth extractions and, in addition, various members of her family had bled to death after fairly trivial trauma. Numerous operations had been performed on the feet as an infant.

On examination.—There are numerous linear scars on the subcutaneous surfaces of both ulnas, extending from the wrists to the elbows. On the back of the right wrist is an incompletely healed wound with a lump the size of a plum underneath it. This is stated to have been a spontaneous split like the others, which has not healed. There are similar scars on the legs on the extensor surfaces and numerous operation scars on the feet. There is marked hyperextensibility of the thumbs of both hands and to a slight degree also of the fingers. It is impossible to say what the state of the feet would normally be owing to the surgical operations which have been performed, nor was it possible to find out for what they were performed. The skin can be said to be hyperelastic over the elbows. No other abnormalities.

Bleeding time 2 minutes. Clotting time 90 seconds. Platelets normal.

Comment.—I was first shown this case by the surgeon under whose care she was admitted, as a possible artefact, which seemed a probable diagnosis, especially in view of the fact that the majority of the scars were on her right side and she was left handed, although the scars were not the typical broad papyraceous type over the knees and elbows, but were fairly linear.

Since Dr. Parkes Weber's paper in 1936 (*Brit. J. Dermat.*, 48, 609) quite a number of cases have been shown or reported in this country. I have no doubt that this is a case of Ehlers-Danlos syndrome.

Of the triad of symptoms, splitting is the only one at all well marked in this case, though the others are present. Excessive bleeding from the mucous membranes such as she describes is not usually a feature of this disease; these is no evidence of any abnormality in her bleeding or clotting time although the wounds as seen had certainly oozed rather more than usual.

Discussion.—Dr. W. FREUDENTHAL: Histologically the nodule situated in the subcutis and extending into the cross-striated muscle below consists of loose, irregularly arranged bundles of connective tissue which has in many places a greatly increased number of cells. The tissue contains a large number of capillary, small and medium-sized blood-vessels and large spaces mostly filled with blood with a scanty endothelial lining and strands of hyaline masses in the neighbourhood. Elastic fibres are almost entirely absent.

Dr. PARKES WEBER: The case is a genuine example of the Ehlers-Danlos syndrome, as it shows the three main features, though to a very minor degree. The splitting of the skin and broad atrophic scarring after traumata are only moderately marked. The "cutis laxa" is present only over the elbows, where it may be seen almost to the same extent in otherwise normal individuals. Over-extension of joints can be obtained only in the thumbs, where it is common (so-called "double-jointed thumbs"). The case is specially interesting, showing, as it does, how lesser forms of this developmental dysplasia are sometimes present in individuals who can be regarded as almost normal.

Chronic Recurrent Herpetiform Stomatitis.—GEOFFREY DUCKWORTH, M.R.C.P.

L. J., a draughtsman, aged 27, has complained of slightly painful ulcers in the mouth for the past six years. He has seldom been free from one or more during this time. The lesions develop as small vesicles, the roofs of which separate leaving superficial ulcers, sharply marginated with a bright red halo. There is no induration, and healing usually occurs in two or three weeks, though occasionally one will persist longer. Scarring does not occur. The tongue, the inner surfaces of the lips, the buccal mucosa, and the palate have all been affected. The floor of the mouth is a favourite site. Fever is unusual. Sometimes the glands, submental and submaxillary, are a little enlarged and tender.

His health otherwise is good, and he has not had any serious illnesses. Six months after the present trouble began he had his teeth seen to and a few metal fillings were inserted. At present his dentist thinks the teeth need no attention.

Scrapings from ulcers showed short-chained streptococci (non-hæmolytic) and a few *M. catarrhalis*, at one time, and Gram-positive lanceolate diplococci (? pneumococci), with a few short chains of streptococci, at another time. No Vincent's organisms have been identified.

The blood picture when last examined was: R.B.C. 4,620,000 per c.mm., Hb. 86%, C.I. 0·93, W.B.C. 7,400 per c.mm., polymorphonuclears 59%, lymphocytes 33%, mononuclears 7%, eosinophils 1%. W.R. negative.

A fractional test meal gave normal curves. An X-ray of the chest showed no evidence of pathological changes in the lungs. The heart's shadow was a little increased on the left side.

Alkaline powders, sedative and tonic mixtures, sulphanilamide, sulphapyridine, nicotinic and ascorbic acids, injections of aneurin, and bismuth, have been given at various times, but no material changes have followed. Locally, sedative applications have been the rule, with occasional applications of phenol. Inoculation of fluid from an early vesicle has not been tried yet.

Discussion.—Dr. L. FORMAN: Sutton, commenting on the results of treatment in two cases of recurrent ulcers of the mouth, stated that the ulcers cleared up more quickly with sulphathiazole than with any other treatment. He thought it the best method he had used for controlling these painful ulcers. ("Recurrent, Scarring, Painful Aphthæ: Amelioration with Sulfathiazole in 2 Cases", Sutton, R. L., 1941, *J. A. M. A.*, **117**, 175.)

Dr. STANNUS: The case might be one of recurrent herpes. Has any effort been made to identify the virus of herpes? This should not be very difficult. Has Dr. Duckworth tested the gastric acidity and are there any blood changes? A condition closely resembling that seen in this case occurs in sprue and some nutritional diseases occasionally seen in this country. Some will clear up with nicotinic acid. The only suggestion I would make is that you combine riboflavin with nicotinic acid.

Dr. DUCKWORTH: The patient has had a fairly long course of M & B 693, and nicotinic acid.

Section of Epidemiology and State Medicine

President—E. H. R. Harries, M.D., M.R.C.P., D.P.H.

[*October* 24, 1941]

The Trend of Fever Hospital Practice

PRESIDENT'S ADDRESS

By E. H. R. Harries, M.D., M.R.C.P., D.P.H.

"Middlemarch," one of the later novels of George Eliot, first published serially in 1871-72, has a certain medical interest because of the allusions to Edward Jenner, Louis, Bichat, Wakley, and others; and to infectious diseases, including the first cholera epidemic of 1831. Middlemarch is a provincial town, and a secondary plot turns upon a new hospital to be provided in addition to the Old Infirmary, and upon a medical man Lydgate. In 1829 Lydgate had at the age of 27 settled in the town fresh from his studies in Edinburgh and Paris, and fired by the work of Louis, whose book on typhoid fever had, of course, appeared in 1829. Opposition to the new hospital was incurred and funds were refused on the score that people preferred to give to the Old Infirmary and thus its construction, mooted in the first "had lingered" into the second volume of the novel. Meanwhile the would-be patron Bulstrode "framed his plan of management". It reads as follows:

"The Hospital was to be reserved for fever in all its forms; Lydgate was to be chief medical superintendent, that he might have free authority to pursue all comparative investigations which his studies, particularly in Paris, had shown him the importance of, the other medical visitors having a consultative influence, but no power to contravene Lydgate's ultimate decisions; and the general management was to be lodged exclusively in the hands of five directors . . . who were to have votes in the ratio of their contributions . . . no mob of small contributors being admitted to a share of government. There was an immediate refusal of every medical man in the town to become a visitor at the Fever Hospital. 'Very well', said Lydgate to Bulstrode, 'we have a capital house-surgeon and dispenser, a clear-headed, neat-handed fellow; we'll get Webbe . . . as good a country practitioner as any of them, to come over twice a week and in case of any exceptional operation, Protheroe will come from Brassing. . . . The plan will flourish in spite of them and then they'll be glad to come in. Things can't last as they are; there must be all sorts of reform soon and then young fellows may be glad to come and study here.'" Lydgate, it is added, was in high spirits which, it must be observed, was unusual for him. In the end, more than 300 pages later, Lydgate leaves the town under an undeserved cloud. He specializes in gout and becomes wealthy, but dies at the age of fifty, surprisingly, but perhaps appropriately enough, of diphtheria.

Although the action of the book passes in the early eighteen-thirties it seems to me not improbable that George Eliot in introducing the theme of a new fever hospital had in mind the hospitalization of the infectious sick, which culminated in the passing of the Sanitary Act of 1866 empowering local authorities to erect and maintain infectious

diseases hospitals, and the Metropolitan Poor Law Act of 1867 which resulted in the constitution of the Metropolitan Asylums Board

However this may be, Murchison (1862) devotes the last chapter of his classic on the "Continued Fevers of Great Britain" based upon his experience as physician to the London Fever Hospital to a discussion on "the relative merits of isolating fever patients and of distributing them in the wards of general hospitals". Some held that "it would be better to have no hospitals at all than to mix cases of typhus, smallpox and scarlet fever with patients suffering from other diseases", while others roundly declared that "fever hospitals and fever wards are at all times a crime against humanity and a disgrace to the age in which we live". A demand was made for the closing of the London Fever Hospital which had been opened with other "houses of recovery" in the provinces and in Ireland at the beginning of the century primarily to cope with epidemics of typhus. Among the conclusions reached by Murchison are that "fever hospitals are absolutely necessary in all large towns liable to epidemics of typhus, and that they ought to be provided with means of rapid extension; that in all general hospitals there should be, where possible, arrangements for the treatment of patients suffering from contagious fevers . . . but these patients ought not to be interspersed through the general wards but isolated in separate wards or better in a detached building". (John Haygarth of Chester had expressed much the same views in 1778.) Cases of enteric fever, however, Murchison thought might be distributed in the wards of a general hospital with impunity. Nor did he see any objection to the many cases of acute non-contagious diseases, constantly being sent in by mistake to fever hospitals, being treated in the same wards with enteric fever. Murchison's arguments for the retention of fever hospitals were received coldly by Simon, who accepted the Report of Bristowe and Holmes (1863). They were of opinion that "scattering the cases is the safest course if the hospital be spacious and the applications not too numerous" (surely a counsel of perfection in the conditions of the times), and emphasized that for safety large well-ventilated wards and beds well removed from each other are essential. Murchison (1864) argued that "whatever plan be adopted, that is [*sic*] mixing or fever wards, the attendants upon patients suffering from smallpox, scarlet fever and typhus must run a certain amount of risk". He pointed out that the objections urged against fever wards were that the concentration of the poison increases among the patients themselves and through the same cause the attendants are endangered. He advocated two thousand cubic feet of space per patient, a standard then obtaining at the London Fever Hospital, but concluded that "however perfect the ventilation of a hospital, smallpox and scarlet fever will spread among persons not protected". Murchison advised separate wards for smallpox, scarlet fever and typhus, because patients convalescent from these diseases are liable to contract the others. Separate wards for these diseases were, however, only introduced at the London Fever Hospital at the beginning of 1862, patients suffering from enteric fever being nursed in the same wards with non-infectious cases; the same "night-chairs" were shared and disinfectants were rarely used. A total of 3,555 enteric fever patients were nursed with 5,144 cases of non-infectious sick at the London Fever Hospital and not one of the latter contracted enteric fever. It may be added that the attendants were not so fortunate.

Murchison (1873) says that since 1862 London had been visited by great epidemics of typhus and relapsing fever, and that to meet the demands for beds the accommodation of the London Fever Hospital—then as now a voluntary hospital—was more than doubled: from 180 beds in 1864 it increased to 364 beds in 1869. During 1864, 2,500 cases of typhus were admitted and this appears to have been the peak year for admissions of this disease. In 1870 the Hospital admitted 631 cases of typhus, 903 of relapsing fever (which had reappeared in 1868, attained its peak in 1869 and finally disappeared in 1872), and 595 of enteric fever. In 1871 all pauper patients were transferred to the "New Fever Asylums", the first of which, the North-Western Hospital, had been opened in 1870 and during that year admitted 218 cases of relapsing fever. The origin of the "New Fever Asylums" is to be found in the great epidemics just mentioned, and the consequent appalling conditions under which the infectious sick were nursed in the London workhouse infirmaries. These conditions, as already mentioned, resulted in the passing of the Poor Law Act of 1867 and the formation of the Metropolitan Asylums Board, merged sixty years later into the London County Council. The M.A.B. was empowered to erect hospitals "for the reception and relief of poor persons who may be infected with or suffering from fever or the disease of smallpox or who may be insane". Until 1883 only

Poor Law patients were admitted: in that year the civil disability was removed by the Local Government Board. Subsequently other infectious diseases were made admissible piecemeal by orders of the L.G.B.

Between 1870 and 1871 three fever hospitals were opened in London just in the nick of time, for the pandemic of smallpox which raged from 1870 to 1874 was, J. D. Rolleston (1937) says in his FitzPatrick Lectures, "the most malignant and extensive outbreak since the introduction of vaccination" (i.e. in 1796). During 1870-74 the new hospitals of the M.A.B. admitted 16,366 cases of smallpox: of these 3,064 were fatal, a case fatality rate of 19%. Although typhus and relapsing fever (one year only) were admissible to the Board's hospitals, the annual numbers did not approach some of Murchison's figures. The highest total was reached in 1874. Thereafter the numbers declined rapidly and the last admissions of typhus (3 cases) were recorded in 1910. *Absit omen!* Goodall (1934) in his "Short History of Epidemic Infectious Diseases" says that in England and Wales enteric fever reached its peak mortality in 1875. In that year 8,913 deaths from enteric fever (besides 1,599 from "continued fever") occurred in England and Wales. Basing his conclusion on a fatality rate of 16%, Goodall assumed that some 56,000 cases of enteric fever must have occurred in the country in that year. Enteric fever declined much more slowly than typhus, and bad years occurred in 1895 and again in 1905, when admissions to the M.A.B. hospitals reached the peak figures of 661 and 586 respectively. It is to be borne in mind that from 1881 until at any rate 1902 it was the practice of the M.A.B. ambulance service to remove, when desired, enteric fever patients from their homes to general hospitals and thus the M.A.B. hospital records only represent a proportion of these patients hospitalized. As late as 1910 the M.A.B. admitted only 51% of the cases of enteric fever notified in London

In 1875 the great Public Health Act was passed and a commencement was made in the abatement of grosser nuisances, and this was the cause of the decline in prevalence of the continued fevers, louse-borne or water-borne, as they are now known to be.

THE CLOSE OF THE FIRST PHASE

The first phase of fever hospital practice which began with the century was drawing to a close. It was the pre-bacteriological era and medical and administrative practice was simple; separate wards, if accommodation permitted, for infectious diseases other than enteric fever, which was nursed with non-infectious diseases of mistaken diagnosis. The ventilation, "which is universally admitted to be necessary for preventing typhus spreading in a general ward was", said Murchison, "injurious to patients suffering from many diseases, such as nephritis, acute rheumatism and bronchitis", and therefore presumably would be discouraged in other than typhus wards. As to the danger to the nurses, Murchison relied upon a supply "protected by a previous attack of typhus or of an age at which it is not very likely to be fatal". Presumably those engaged in nursing smallpox were vaccinated, and although Murchison distrusted scarlet fever (diphtheria is not mentioned) he appeared to be unduly optimistic about enteric fever. Nowadays, of course, it is the usual practice to protect the nursing staff not only against smallpox, but to immunize them against diphtheria (Harries, 1930) and scarlet fever (Harries, 1935) and the enteric group of fevers. Recently, too, selected members of the staff of my own hospital have been inoculated against epidemic typhus.

THE OPENING OF THE SECOND PHASE

The second phase of fever hospital practice opens in the 'eighties, which also saw the commencement of the bacteriological era (Eberth, typhoid bacillus, 1880; Klebs, diphtheria bacillus, 1882; and Klein, streptococcus, 1887). For the next thirty or forty years fever hospital practice was dominated by scarlet fever; for smallpox, of course, then as now, separate provision was made. In 1882 Thorne observed that "scarlet fever had rarely been the immediate cause of hospital provision and this notwithstanding the fact that the mortality it occasions has been so greatly in excess of that resulting from smallpox". From 1866 until 1880 only some thirty local authority hospitals had been provided but Franklin Parsons (1914) remarks that during the course of the next two decades scarlet fever had come to be looked upon as the disease *par excellence* requiring hospital isolation. Some hospitals were reserved exclusively for it, more urgent cases of diphtheria and enteric fever not being admitted, and "in most isolation hospitals cases of scarlet fever formed the great majority of those treated". From 1881 to 1890 101 isolation

hospitals were provided; 181 from 1891 to 1900, and 216 from 1901 to 1910, i.e. a total of nearly 500 in thirty years (A. C. Parsons, 1927). Nearly always these hospitals were erected upon the outskirts of towns in deference to public opinion. What were then the outskirts have now in many cases become built-up areas embedding the fever hospital, which its neighbours regard with complete composure. In point of design these structures might range from "a tarred shed of repulsive appearance such as had sufficed for small-pox" (Thorne), to permanent hospitals "deficient in important respects such as cubic space, means of separation of different diseases and accommodation for staff" (Parsons, 1914).

From 1,100 admissions of scarlet fever to the M.A.B. hospitals in 1875 the numbers rose to nearly 17,000 in 1905 (nearly 18,000 in 1906); in 1915, 15,000 cases were admitted and in 1935 there were 10,700 admissions to the hospitals of the L.C.C. But whereas the case fatality rate in 1875 was 13·7% (probably selection on grounds of clinical severity and concomitant diphtheria contributed), it was in 1935 only 0·25% in spite of selection. C. V. Chapin (1926) thought that in England the decrease in severity of scarlet fever ran closely parallel to the development of isolation and that the change in type from severe to mild was influenced by the isolation of the majority of serious cases. Rolleston (1937) points out that the maximum mortality was reached in 1863, and Parsons (1927) shows that the decline in both mortality and fatality which began about 1875 preceded not only compulsory notification but also the general provision of hospital facilities, and that the commencement of this decline synchronizes with the passing of the Public Health Act, 1875. But whereas the continued fevers declined in prevalence from the date of passing this Act, prevalence of scarlet fever has remained practically undiminished.

Greenwood (1927) concluded that "it has not been proved that with the epidemiological type of scarlet fever seen in this country during the last twenty years hospital isolation has had any effect, good or bad, upon prevalence, or any substantial effect upon mortality or fatality. This is not to say", he adds, "that if we had been dealing with the scarlet fever of sixty years ago with a more than tenfold mortality we should have reached the same conclusion".

It became the practice in many towns, and this practice obtained until very recent years, to hospitalize the highest possible percentage of notified cases of scarlet fever with the result that the wards became overcrowded and the nursing staff overworked. The overcrowding was made worse by the length of stay which was primarily determined by the absolute completion of desquamation, and it was never less than six weeks. The effects of overcrowding and long stay were high complication rates which raised the average length of stay still more. In other words a vicious circle was established. Inadequate isolation favoured "cross-infection" and return cases and in the late 'nineties there was public outcry. The position was well stated by Parkes (1903): "The existing fever hospital is certainly 'isolation' so far as the great body of the public is concerned, but is in no sense isolation of the sufferer amongst his fellow sufferers."

That this view was fully shared by contemporary medical officers of health and the medical superintendents of the large fever hospitals is shown by the numerous references to the subject in the public health literature of the period. Twenty years before the recognition of the causal organism of scarlet fever by the Dicks (1923) (the streptococcus had of course been more than suspected by Klein in 1887), it was recognized by fever hospital clinicians that patients suffering from the septic type of scarlet fever—now very rarely encountered—were potential sources of infection for other patients in scarlet fever wards. This is clearly brought out by A. G. R. Cameron (1904) in his well-known report upon return cases of scarlet fever. Infective discharges from nose or ear might, he concludes, be conveyed "directly from other patients or indirectly by attendants, toys, utensils, or dust". This was, of course, "cross-infection", and thanks to the work of the late F. Griffith (1926) and its practical application to scarlet fever wards by Allison (1937), and others, it is now known frequently to be caused by other serological types of hæmolytic streptococcus. Cross-infection in its primitive sense of an extraneous infection resulting in a clinical attack of a second acute specific fever was and is a major problem for the medical administrator of fever hospitals, many of which are still deficient in isolation accommodation. Attempts were made at a partial solution of the problem by subdivision of existing structures into cubicles or chambers, and the introduction of an antiseptic or aseptic technique or a combination of both. Some of these methods are described in the Milroy Lectures (Harries, 1935).

As is well known, they are based upon the experience of Grancher and Hutinel in Paris, which culminated in the opening of the Pasteur Hospital (*l'hôpital cellulaire*) in 1900. It is interesting to recall in the light of current work on cross-infection that Grancher and Hutinel, when they devised their screens and boxes, were concerned not so much about the transference of the acute specific infections but of the non-specific infections caused by the streptococcus which Hutinel forty-five years ago recognized as the chief enemy of children in hospital. Knyvett Gordon (1905) considered that the extent to which superadded disease occurs in a hospital is in a large degree the measure of its efficiency; he was very sceptical about aerial convection, but very definite about dirty hands; advocated isolation of doubtful cases for three weeks; and instituted a strict aseptic technique. Gordon Pugh (1906) first reproduced Hutinel's boxes at the North-Eastern Hospital, at that time and for many years afterwards, seriously deficient in isolation accommodation. These boxes were only demolished to make room for new blocks just before the war.

Goodall (1906) complained that his "most valuable" isolation accommodation at the Eastern Hospital (then containing 368 beds, but since enlarged) consisted of a block of six single-bedded rooms and a kitchen; the rooms usually, perforce, housed two patients each. This isolation accommodation was less than 2% of the total number of beds, and four years later Goodall (1910) reports the division of a ward into completely separate chambers. In 1908 Biernacki of the Plaistow Fever Hospital recorded the results of barrier nursing patients with septic scarlet fever in the same ward with those suffering from the simple type, using coloured cords to indicate the barriered patients. Caiger (1910) assessed the value and limitations of the cubicle system at the South-Western Hospital. Open wards had been converted into cubicles at the expense of scarlet fever accommodation. Next came the system of bed isolation or the "invisible barrier" based upon spacing, ventilation, the control of dust by damp sweeping and dusting and a strict aseptic technique. Crookshank (1910) and Rundle (1912), the pioneers of bed isolation, both read papers before this Section. Crookshank insisted that every detail of the isolation ward should be on a parity with the best surgical wards. It is pertinent to observe that with certain additions such as masking, the technique now adopted to diminish "hospital infections" in surgical wards is *mutatis mutandis* essentially that first employed in bed isolation wards thirty years ago, and this, in turn, was derived from the surgeons. C. V. Chapin (1912), whose "Sources and Modes of Infection" (1910) is a minor classic of preventive medicine, discarded all paraphernalia such as gowns, gloves, disinfectants and fumigation and relied upon simple cleanliness at Providence City Hospital. He believed "the wonderful success of the Pasteur Hospital to be largely due to the employment of a skilled permanent staff". With this all will agree who have had to conduct any form of barrier nursing. Thomson (1916) indeed had during the last war to suspend his work on the aerial conveyance of infection in wards "owing to shortage in the type of nursing staff capable of the high standard necessitated by the work". I was privileged to work in Rundle's first bed isolation ward and later found bed isolation, with all its admitted limitations, of very great value during many years as a supplement to the then scanty isolation accommodation in Birmingham—but the staff had to be picked and experienced in surgical asepsis, otherwise avoidable cross-infections tended to occur.

Diphtheria was first admitted to the M.A.B. hospitals in 1888. In that year only 99 patients were received, and of these 46 died, a case fatality rate of 46·5%. The annual admissions increased rapidly after the Infectious Diseases Notification Act, 1890. In 1894 there were 3,666 admissions, with 1,035 deaths (case fatality rate 28·2%). It was in this year that Goodall received sufficient diphtheria antitoxin from Lister, who obtained it from Roux, to treat 20 patients at the Eastern Hospital. In 1895 antitoxin was in general use in the M.A.B. hospitals and the case fatality rate fell to 22·8%. 1909 was the first year in which the so-called "bacteriological diphtheria" (a contradiction in terms) was separated statistically in the M.A.B. reports and, it is to be hoped, physically in the M.A.B. hospitals. In 1909 cases of bacteriological diphtheria constituted roughly 5% of the total number of admissions. In 1925 such cases formed approximately 10%, and in 1935 the proportion, viz. 9%, was still much the same. These London percentages are low compared with those of some of the provincial fever hospitals. In my own experience in Birmingham, one-third of the notified cases of diphtheria in some years might present no clinical evidence of the disease. I need not enlarge upon the fallacies and tragedies of the swab diagnosis of diphtheria. A proportion of these patients are, of course, immune carriers. Thomson and his co-workers (1925, 1926) carried out a considerable

investigaton on diphtheria carriers, and as a result a carrier clinic has been maintained at the North-Eastern Hospital ever since. Especially in the case of release cultures, the use of selective tellurite media, the relentless search for the ultimate diphtheria bacillus, cause increased difficulties for the fever hospital clinician. Time marches on, and the child who enters a hospital harbouring a few diphtheria bacilli, to the toxin of which he can frequently be shown immune by the Schick test may remain many weeks before he attains bacteriological righteousness as determined by modern media. In my own hospital we have arrived at a compromise: tellurite plates for confirmatory diagnosis and Löffler medium for release cultures. I am sure that this procedure does not result in an undue acceleration of the first of the "velocities of infection" postulated by Sheldon Dudley (1926).

THE THIRD PHASE

The third phase of fever hospital practice may be said to commence during the first decade of the present century. From 1888 scarlet fever, diphtheria and enteric fever were the three notifiable diseases, other than smallpox, admitted to the M.A.B. hospitals. But Cuff (1910) reported upon the desirability of using some of the spare accommodation in the fever hospitals for the treatment of measles, whooping-cough and puerperal fever. As a result the M.A.B. fever hospitals were gradually brought into line with those in such cities as Glasgow, Edinburgh, and Liverpool. Glasgow had admitted measles since 1891, Edinburgh for some years, and Liverpool measles and whooping-cough from 1908. In Edinburgh puerperal fever was treated in the same ward as enteric fever. It was actually the admission of puerperal fever, erysipelas and infectious enteritis, among other additional infectious diseases, that led to the institution of bed isolation in Liverpool. Fazakerley Hospital at that time was new and possessed isolation accommodation sufficient for its ordinary practice, but the widened clinical field necessitated an increase, and bed isolation met the need without structural alterations or additions. Cuff recognized that the admission of measles and whooping-cough would be for curative rather than preventive reasons and, surprisingly, had to allay fears that these diseases might spread from ward to ward on the analogy no doubt of the alleged aerial convection of smallpox over considerable distances. Measles and whooping-cough were admitted to the M.A.B. hospitals at first to such accommodation as could be spared after the prior claims of diphtheria and scarlet fever had been satisfied. Only in 1926 were these diseases admitted on equal terms with scarlet fever, and in 1930 the L.C.C. provided for cases of measles in fever hospitals which hitherto would have gone to Poor Law Infirmaries. The successive epidemics of measles in London during recent years and the steps taken by the L.C.C. to meet the demands for hospitalization have been described in the well-known series of reports by the Council's Medical Officer, and Brincker (1932, 1936) has published several papers upon the control of measles in London. In 1936 the following table (quoted from the Annual Report of the Medical Officer, London County Council (1936), vol. IV, Part I) gives an indication of the practice of the L.C.C. fever hospitals in a pre-war year:

Disease	Admissions	Case mortality percentage*
Diphtheria	5,154	4·06
Diphtheria carriers	404	0·24
Scarlet fever	9,304	0·36
Enteric fever	117	9·61
Puerperal fever and pyrexia	181	8·17
Measles	12,788	3·98
Whooping-cough	2,774	8·41
Other diseases	7,881	3·44
Total	38,693	Total 3·31

* According to principal disease diagnosed on admission (not necessarily cause of death).

In 1937 the nomenclature of the acute specific infectious diseases admissible to the L.C.C. fever hospitals was revised and 28 different diseases were enumerated. With the exception of exotics such as plague and cholera, few of the diseases named in this list are unrepresented among the "other diseases" accepted for admission during a year. Earlier in this Address I remarked upon the vicious circle which had been established in the case of scarlet fever as a result of long stay and overcrowding tending to a high complication-rate and cross-infection; as late as 1910 Cuff noted that the average length of stay of scarlet fever patients in the hospitals of the M.A.B. was nine weeks. Many of

these patients were transferred to convalescent hospitals for the completion of desquamation, thus making room for more patients in the acute hospitals but tending to prolong the average length of stay.

During the last twenty years or so the duration of stay of patients in general, and of scarlet fever patients in particular, in many fever hospitals has been reduced very considerably. The traditional period of detention of six weeks is now four weeks or less for the uncomplicated case of scarlet fever, with, of course, a reduction in the average length of stay. Return case-rates have certainly not increased as a result of the shorter stay; in fact, return cases appear now to be few and far between, judging from the experience in my own hospital. The factors which have brought about this shortened period of stay with consequent release of beds for other diseases may be enumerated as follows:

(1) The mildness of the disease with few cases of septic type.

(2) The use of scarlet fever antitoxin, and possibly the sulphonamides, which brings more cases into the category of "uncomplicated" and diminishes desquamation, which in any case has long been disregarded as a source of infection.

(3) Maintenance of proper spacing (12 ft. of wall space) and avoidance of encroachment upon this spacing even in times of prevalence, shown to be equally important by J. A. Glover (1932, 1934) in other environments.

(4) Segregation by one of the means already mentioned of children who are likely to disseminate other serological types of the hæmolytic streptococcus, i.e. children with unhealthy conditions of the nose, throat or ear.

(5) Specialized treatment of such children by otologists combined with bacteriological control, thus preventing permanent damage to the ear, and shortening the length of stay without the danger of releasing children with grossly infective foci. (Release cultures are not ordinarily obtained prior to discharge of the uncomplicated case of scarlet fever.)

ISOLATION

In 1926 Caiger represented to the M.A.B. that isolation should be provided to the extent of one-third of the total accommodation of the acute fever hospital and one-fifth in the case of convalescent hospitals. This standard was adopted by the L.C.C. and it was resolved that isolation should take the form of single glass chambers. Up to the outbreak of the war several of the Council's acute fever hospitals had been provided with isolation blocks of this type, but the North-Eastern Hospital was fortunate inasmuch as an extensive reconstruction was completed just before this war commenced. As a result more than one-third of the total accommodation of 760 beds consists of isolation in the form of one or two-bedded chambers. Two blocks contain between them 112 single chambers and one-third of each of eight new two-storied blocks consists of one or two-bedded glass chambers.

Among other new structures provided were receiving rooms, a discharge block, a theatre suite, X-ray and ultra-violet ray departments, laboratories and lecture room. In short, the North-Eastern Hospital at the outbreak of war could challenge comparison in the matter of wards and equipment with any hospital in the country devoted to special diseases. But after all, the work of a hospital does not depend upon buildings. Good work had been done by my predecessors during many years under great difficulties in the old huts which these new structures displaced. Lack of isolation accommodation was their greatest defect. I have already alluded to the work of otologists in fever hospitals. They were first appointed in the 'twenties in Edinburgh, and then in London (Layton, 1921, 1924), Newcastle-on-Tyne and Birmingham in that order. But in London and in most large cities fever hospitals can now call upon the assistance not only of otologists but of specialists and consultants in any branch of medicine or surgery. Thus fever hospitals are in many cases now entitled to equal rank with other special hospitals. They are even acquiring a tradition which has grown out of the life-work of such men as Claude Ker and E. W. Goodall, to name only two. The old dread of the public has disappeared, and the modern fever hospital is accepted as a necessary social amenity. If anything, it has become popular, and this says much for its "atmosphere" which is, or should be, that of a children's hospital.

REFERENCES

ALLISON, V. D., and BROWN, W. A. (1937), *J. Hyg.*, **37**, 153.
BIERNACKI, J. (1908), *Nursing Times*, **4**, 373.
BRINCKER, J. A. H. (1932), *J. Roy. San. Inst.*, **53**, 108.
Id. (1936), *Lancet* (i), 103.

BRISTOWE, J. S., and HOLMES, T. (1863), in 6th Rep. of M.O. of Privy Council.
CAIGER, F. F. (1910), *Pub. Health*, **24**, 336.
CAMERON, A. G. R. (1904), Rep. to M.A.B. on Return Cases of Scarlet Fever and Diphtheria.
CHAPIN, C. V. (1910), "Sources and Modes of Infection". New York.
Id. (1912), *Am. J. Pub. Health*, **2**, 135.
Id. (1926), *J. Prev. Med.*, **1**, 1.
CROOKSHANK, F. G. (1910), *Proc. Roy. Soc. Med.*, **3** (Sect. Epidem., 73).
CUFF, H. E. (1910), *M.A.B. Ann. Rep.* (Med. Suppl.), 279.
DICK, G. F., and DICK, G. H. (1923), *J. A. M. A.*, **81**, 1166.
DUDLEY, S. F. (1926), Med. Res. Counc. Spec. Rep. Ser., No. 111.
GLOVER, J. A. (1932), *Proc. Roy. Soc. Med.*, **25**, 1783.
Id. (1934), *Tr. M. Soc. London*, **57**, 75.
GOODALL, E. W. (1906), *M.A.B. Ann. Rep.*, 216.
Id. (1910), *ibid.* (Med. Suppl.), 257.
Id. (1934), "A Short History of the Epidemic Infectious Diseases". London.
GORDON, KNYVETT (1905), *Pub. Health*, **17**, 384.
GREENWOOD, M. (1927), *Rep. Pub. Health & M. Subj.*, No. 35 (Ed. Parsons, A. C.).
GRIFFITH, F. (1926), *J. Hyg.*, **25**, 385.
HARRIES, E. H. R. (1930), *Lancet* (i), 830.
Id. (1935), *ibid.* (ii), 173, 233.
LAYTON, T. B. (1921), *M.A.B. Ann. Rep.*, 76.
Id. (1924), *ibid.*, 187.
MURCHISON, C. (1862), "The Continued Fevers of Great Britain". London, 2nd Ed. 1873. 3rd Ed. 1884 (Ed. Cayley).
Id. (1864), *M. Times*, **1**, 210.
PARKES, L. C. (1903), *Pub. Health*, **15**, 538.
PARSONS, A. C. (1927), *Rep. Pub. Health & M. Subj.*, No. 35.
PARSONS, H. FRANKLIN (1914), "Isolation Hospitals". Cambridge.
PUGH, W. G. T. (1906), *M.A.B. Ann. Rep.*, 6.
ROLLESTON, J. D. (1937), "The History of the Acute Exanthemata". London.
RUNDLE, C. (1912), *Proc. Roy. Soc. Med.*, **5** (Sect. Epidem., 171).
THOMSON, F. H. (1916), *Lancet* (i), 341.
THOMSON, F. H., MANN, E. J., and MCCARTNEY, J. E. (1925), *M.A.B. Ann. Rep.*, 130.
THOMSON, F. H., MANN, E. J., MCCARTNEY, J. E., and HARVEY, W. C. (1926), *ibid.*, 214.
THORNE, R. T. (1882), Suppl. 10th Ann. Rep. L.G.B.

Section for the Study of Disease in Children

President—A. G. Maitland-Jones, O.B.E., M.D.

[*November* 28, 1941]

DISCUSSION ON THE EFFECTS OF WAR-TIME RATIONING ON CHILD HEALTH

Dr. E. M. Widdowson: Unpublished data which were obtained in a dietary survey, carried out during the years 1935-1939, on 1,000 individual middle-class children have been used to determine the pre-war intakes of foods that are now rationed. A comparison of these intakes with the actual rations to-day gives a fair idea of how the present system of rationing has or has not cut across middle-class children's dietary habits. It was found that the rations provide children up to 8 years with as much meat, bacon, sugar and jam as they were having before the war. Children over 8 years were formerly eating more of all these foods, and adolescent boys were eating two to three times as much as their present rations provide. The average pre-war intake of butter was more at all ages than a ration of 2 oz. per week, while the mean consumption of cheese was always very much less than the present weekly allowance of 3 oz.

It is suggested that, in spite of the dietary restrictions to which older children have had to submit, appetite and instinct will have led them to maintain their calories by an increased consumption of bread, potatoes and other plentiful foods. The adolescents' loss of protein, iron and vitamin B_1, brought about by the rationing of meat and bacon, can readily be made good by an increased consumption of National wheatmeal or wholemeal bread. So long as they receive their full domestic milk allowance, together with ⅓ pint of school milk a day, and if they eat their full ration of cheese, there is no reason why school children's calcium intakes should fall below the corresponding pre-war figures. The calcium available for boys and girls who leave school at 14 or 15 years may, however, be inadequate. If the margarine is vitaminized so that it is equal to summer butter, children up to the age of 12 years can obtain more of the fat-soluble vitamins from their present rations than they had from the same foods before the war. If the margarine is not vitaminized they will get less of these vitamins at all ages above 1 year. Vitamin C intakes have been severely curtailed as a result of the shortage of fruit. It is not known whether this is a serious matter or not.

Dr. Dagmar Curjel Wilson: It is important to appreciate the difference between examination for signs of malnutrition carried out during routine school inspection, and the use of growing children as indicators for the detection of signs of dietary deficiency within a community. Until recently in this country the clinical signs of deficient intake, apart from the malabsorption due to organic defect, have received but little attention. Yet, as Lord Horder says, dietary deficiency may leave scars on our people even before its presence is recognized.

During school medical inspection the state of nutrition is assessed according to the standards laid down by the Board of Education, in order primarily to benefit the individual child. Such examination is largely subjective, and the results of different observers are not comparable. It is, however, useful in drawing attention to the many different

causes in home and school life which may adversely affect the child's well-being and lead to increased liability to infection; and thus permits of application of appropriate remedy. Accurate height and weight records, taken of individual children at regular intervals, may supply additional evidence of how far from optimum is the nutritional state of the so-called "normal" child.

For the early detection of specific dietary deficiency within any communal group, special tests are necessary. It is a matter of opinion how such examination is best carried out, whether on limited clinical material in a highly equipped laboratory, or by the application of selected tests on large numbers in the field.

For four years previous to the outbreak of war, I held under the Royal Society, an appointment for nutritional research in India. During this time I worked in close co-operation with Dr. W. R. Aykroyd and the staff of the Nutritional Research Laboratory at Coonoor. India offers particularly favourable conditions for dietary investigation, since it is possible to study populations maintaining their customary diets at many different nutritional levels, and thus to correlate deficiency disease with dietary intake. Indian experience shows that after careful laboratory investigation of clinical cases showing signs of dietary deficiency, the trained worker gains sufficient knowledge to go out to distant areas and apply selected, standardized clinical tests in the field.

That some conditions easily recognized by such tests are closely related to deficient intake of essential food factors was shown by dietary surveys worked up later with Dr. Widdowson in the Department of Medicine at Cambridge. During the past two years I have looked for the same conditions amongst groups of rural English school children. The existence amongst them of a slight degree of dietary deficiency was indicated by the occurrence of cheilosis and of low-grade rickets. It seems probable that more signs of deficiency would have been found but for the widespread provision of milk in schools. The results of this inquiry have been summarized recently in the *Lancet*, 1941 (ii), 405.

The signs of dietary deficiency applicable under war-time conditions in English schools are:

Follicular hyperkeratosis.—Keratinization in and around the pilosebaceous follicles of the skin is readily noted. In India the same standard of skin roughness to the examining finger-tip has been maintained in all dietary surveys, the degree of roughness recorded is similar to that described by Nicholls in Ceylon as "phrynoderma" or toadskin. This is probably not a simple vitamin A deficiency. Dr. Widdowson and I found on analysis of my Indian records that in addition to specific dietary deficiency, other unfavourable dietetic conditions or unhealthy surroundings are necessary before the disease becomes manifest.

Angular stomatitis.—Various observers have described ulceration of the mouth associated with deficient diets. Sebrell and Butler considered cheilosis as evidence of riboflavin deficiency. Varying results, however, have been obtained on treatment in different parts of the world, which Stannus has suggested may be explained by the absence of different essential factors in the enzyme system with which the vitamin B_2 complex is concerned.

Angular stomatitis is convenient for record, though a similar appearance may be seen at other sites where skin and mucous membrane meet. The extent of the white patches of epithelium at the corners of the mouth may vary considerably, and closer inspection often reveals an ulcerated surface in addition.

Xerosis and keratomalacia.—There is loss of lustre and wrinkling of the bulbar conjunctiva, and accumulations of epithelium, white or foam-like in appearance, which usually appear first to the outer side of the cornea, and form Bitot's spots, an easily recognized sign of vitamin A deficiency. We do not always recall that Bitot also noted that many of the children who showed these ocular conditions were living largely on carbohydrate and had a plump appearance.

Bleeding gums.—While all agree as to the desirability of an optimum intake of vitamin C, it is well in these times of dietary restriction to be able to recognize minimum requirements. I had an opportunity of examining 500 children aged from 5 to 15 years, chosen at random from large numbers in a famine relief camp in North India. Though purple discoloration was noted, no bleeding from the gums was detected. For the past three months the diet had contained no oil or fat but had consisted of whole wheat coarsely ground and about half an ounce of fresh green chillies daily, which would provide about 15 mg. of ascorbic acid. It is interesting to note that Zilva and Kellie as the result of

their laboratory findings, suggested that a daily dose of about 15 mg. of ascorbic acid should be sufficient to meet the theoretical requirements of man.

Rickets.—The slighter and earlier signs of vitamin D deficiency may be recognized in the epiphyses at wrist and ankle, and are worthy of record. Very often further inquiry in home or school will show another member of the same family with more definite rachitic deformity.

Dr. Helen M. M. Mackay: In any attempt to arrive at general conclusions as to war-time feeding we must bear in mind that food conditions have differed widely at different periods as well as in different areas, and for different groups of children since the beginning of the war; and what is true of food supplies at one time and place may not be true in the next district or even in the next school. Dr. Widdowson has shown in her graphs quantities of rationed food which, on paper, are available to-day for children. I have none of the exact figures that she is able to show for pre-war children, but I am daily questioning mothers as to the feeding of their children, and this experience gives me a much less reassuring picture than that which has just been drawn. Dr. Widdowson has scarcely mentioned eggs, fish, rabbit, chicken and other forms of unrationed meat, all of which figured largely in children's pre-war diets, and are now in short supply. Some wives of Service men cannot afford to buy their share of available foodstuffs. Distribution has often been very uneven. Liquid milk has provided, I think, to the present date an outstanding example of unsatisfactory distribution in children's homes, and milk is, of course, a food of primary importance. Not only that, but some schools provide no milk, and children may spend their halfpennies on sweets and so get no school milk even when it is available. Certainly very few of the school children whom I see are getting 7 pints of milk weekly, though one hopes that the new priority arrangements may effect a considerable improvement soon. Unrationed carbohydrates, particularly white bread, must be consumed in much larger quantities by children to-day than pre-war. Perhaps too, when considering the availability of foods, one might mention breast-milk. Is there a general reduction in the number of mothers able to provide their babies with breast-milk? In the maternity hospital with which I am connected there was a marked falling off in lactation this year.

Suppose an American observer, over here to report on the effects of war-time rationing on child health, asked for information from which to compile his report what could we tell him? That we are thankful that we have had no devastating epidemics so far, though what with war-time feeding and shelter life and disorganization from bombs, we had expected them; that many people have the impression that evacuees in country districts are improving in looks, and that there are no reports published in the journals of large increases in deficiency diseases. But if he said he wanted more precise facts I wonder how many we could give him. Although individuals have made valuable contributions to our information, as witness the two speakers whom we have just heard, yet it is, I think, impossible at present to get any broad view of the effects of war-time diets on children on account of the paucity of available facts. Is, for example, the impression that evacuated children improve in health in part accounted for by the return to the cities of the sickly children? In London hospitals we see a lot of poor specimens back from the country, which makes one wonder. Can anyone here help us with facts on this point?

To guide policy and safeguard the well-being of children more official information is required. If lowered resistance to infection results from most dietetic deficiencies, then publication of the death-rates of children at different ages is badly needed. The wide use of chemotherapy should have brought about a material fall in mortality, particularly from respiratory disease. If this has not occurred, what are the counter-balancing causes? The last analysed figures from the office of the Registrar-General are, I think, for 1937, and we are left guessing as to the trends of mortality figures during the two and a quarter years of war. In the last war there was a large increase of tuberculosis in Germany, acknowledged, I think, to be mainly due to inadequate food. At the Queen's Hospital for Children the proportion of tuberculous children we see nowadays is much greater than in peace-time. From what we hear from other pædiatricians and from doctors in the Public Health Service in different parts of the country, there is a wide impression that tuberculosis in children is increasing. One may try to guess how much of this is due respectively to the wholesale discharge from sanatoria of cases of open tuberculosis at the beginning of the war, or to the consumption of unboiled tubercle-infected milk by city

evacuees accustomed to pasteurized milk, or to lowered resistance from dietetic defects, but at present it is only guesswork, for we do not even know whether the increase is general, or, if so, its magnitude. The subjective classification of nutrition as fair, good, &c., by a variety of observers is of no use for comparison of groups. The school medical officer is required to place the children of the batch he is inspecting into certain groups, and having put a few into the best and worst classes, the rest go into the intermediate groups. But average rate of growth is one of the important indices of the adequacy of the diet, though it may of course be influenced by many other factors. A comparison of average weights of children pre-war and now would not be a simple procedure, since it would involve a comparison of both country and city groups, with due regard, for example, to possible falsification of figures from the return of children in poor health to their own homes from billets. Nevertheless, with the co-operation of statisticians, clinicians and public health officials, useful figures should be obtainable. The survey should, if possible, include adolescents, for these groups in particular, as Dr. Widdowson has demonstrated, are having their usual foodstuffs drastically curtailed, and I fear they may not get enough animal protein to allow of normal growth.

One deficiency disease, nutritional anæmia, is certainly extremely common among infants and young children. I believe there has been a large increase in this anæmia in London in the last two years. Say twelve years ago, severe anæmia was common at this age; but in the East End of London in the immediate pre-war years, though there were plenty of children with their hæmoglobin in the seventies, it had become difficult to find cases of severe anæmia, as I well know, for I hunted for cases for certain therapeutic trials. Now these cases are again common. Dr. Wills and Lady Bingham from the Royal Free Hospital, and Dr. Dobbs and myself from the Queen's Hospital for Children, are trying to get objective evidence of the incidence of anæmia in various groups of supposedly healthy women and children: so far we have not had the opportunity of examining school children. Of the children between 6 months and 4 years old already examined, only about one in six reaches the level of 85% on the Haldane scale, and one in nineteen is severely anæmic, i.e. has a hæmoglobin in the fifties or lower. Babies whose hæmoglobin level averages about 72% have a greatly increased susceptibility to infection. Is it not a reflection on our common sense that we let this anæmia exist? Is it wise to impose a purchase tax on the substance needed for the control of a deficiency disease affecting the majority of our young children? The average hæmoglobin level of these children could be raised to over 80% and the incidence of infection among them drastically lowered, by the simple means of regular iron administration. Dr. Sheldon commented the other day on the very different prognosis for an anæmic baby and for a baby of normal hæmoglobin level if both get bronchitis. We can be sure that respiratory infections are going to be a serious problem among the small children congregated together in day and residential nurseries. Young mothers won't stay in the factories if their babies are ill, therefore on the score of wasted woman-power alone we would do well to look to the health of these infants, and raise their resistance by giving them iron.

Turning to other deficiency diseases, I speak from impression alone. I think there was some increase in the incidence of rickets in London last winter. I have seen no cases of scurvy during the past year, and ascorbic acid seems to be widely used in London to replace orange juice for babies. Vitamin C deficiency is probably commoner in children past infancy than in babies in London. I do not think there is any increase in cases of angular stomatitis or gingivitis in my out-patient clinics. Not long ago, however, I was asked to see a group of children suffering from gingivitis. All were refugees housed in a large building with communal feeding. The children affected were almost all of school age, though no school had been open to them for most of their time in the hostel—and no school meant no school milk. Children under 5 who got more milk escaped: hence the condition was primarily dietetic in origin. The affected children all had gingivitis and conjunctivitis, some had Vincent's angina, some had angular stomatitis. Most had scars of healed sores on their bodies and looked in poor health. The diet probably had multiple deficiencies, but riboflavin deficiency seemed, I think, the most likely to account for the symptoms observed.

The opener of the discussion has shown in a previous paper how war-time rationing has cut right across the feeding habits of men. When there are food shortages, preconceived ideas and the wife's care for the health of the wage-earner play a large part in deter-

mining how the food available will be distributed among members of the family. Often young children get all the—very few—eggs available, and much of the butter; but in many families they tend to be deprived of their cheese and their bacon and perhaps of most of their meat in favour of their elders, particularly the father. The other day I was remonstrating with a mother for giving most of her rationed food to her husband and children only to be met with the reply: "Well it's only human nature." The campaign in favour of well-balanced school meals for children is deserving of strong support, but cannot something be done on similar lines and at very cheap rates for mothers and young children? I suggest, too, that it behoves us to keep constant watch on the feeding provided in hospitals and residential institutions for children, for I suspect that the working-class mother, with all her handicaps and her lack of scientific knowledge, often feeds her children better than does the institution. All honour to her achievement.

Dr. W. W. Payne described an investigation of children to determine the minimal dose of vitamin C in the form of black-currant purée required to supplement adequately the routine diet in an E.M.S. hospital. The children, who were all convalescent cases, were saturated with ascorbic acid either synthetic (50 mg.) or as black-currant purée (1½ oz., equivalent to 40 mg.). Ascorbic acid in the form of black-currant purée was then given as a dietary supplement and the level at which saturation could be maintained was determined by the urinary response to a test dose of ascorbic acid. This level was found to vary from 15 to 6 mg. per stone according to age, corresponding to average daily doses of 1½ to 2 oz. purée per child. For full details of the investigation *see* Payne, W. W., and Topley, E. (1941), *Lancet* (ii), 596.

Dr. J. A. Glover said that his personal impression was that, so far and speaking generally, neither the health nor the nutrition nor indeed the spirits of the elementary school child had deteriorated. There were, perhaps, special areas where an exception might be made. The school child started this war a bigger and better nurtured child than his predecessor of 1914 who had improved on the whole during the last war. It was impossible to disentangle the effects of rationing from those of the many other abnormal factors which had influenced his nutrition in war-time.

Evacuation, often more than once, closure of schools, shorter school hours, smaller classes, shelter-life—these factors with city children, and with all children, such factors as higher wages in the home and the black-out, had for better or worse, affected the nutrition of the school child as well as rationing, though school closure was practically over before rationing began.

The majority opinion of school doctors and nurses, and of teachers was, he thought, against any deterioration in nutrition having so far occurred.

Few knew better than he did the pitfalls of statistics of the clinical assessment of nutrition, but for what they were worth, the aggregate returns of the six years' assessment of nutrition of the children seen each year at routine medical inspections (a yearly average of about one and a half million children) showed no deterioration.[1]

Owing to war-time shortage of staff, figures for average measurements were hard to get for 1940.

He would have expected some decrease in average weights with the rationing of fats, jam and sugar but the evidence of the few areas for which 1940 averages were obtainable was evenly divided. The decreased incidence of infectious diseases in 1940 was indirect evidence against deterioration.

Rationing had greatly accentuated the inadequacy of the "brought lunch", the dinner which the "long distance" child in rural districts brought with him to eat in school.

The Board of Education and the Ministry of Food were doing their utmost by liberal grants in aid, special concessions to school canteens, and persuasion to induce local education authorities to provide dinners and milk in school for every school child.

It is to be hoped that one good result of the war will be the inclusion of the school dinner as an essential part of the school curriculum and the provision of school milk for every child.

[1] A table was shown at the meeting which included some official figures not yet published.

Prof. A. St. G. Huggett: The treatment and care of the infant really begin before birth. The development *in utero* is ultimately dependent upon the food supply of the mother. The effect of restriction is shown by animal experiments and human observations. In proportion to the severity of the deficiency, there is seen: (i) Depletion of maternal food reserves; (ii) loss of maternal weight; (iii) depletion of the fœtal food reserves, and (iv) loss of fœtal weight (low birth-weight). This last is only seen with severe shortage. A limited comparison (of no statistical value) of the birth-weights of the first six months of 1941 and 1938, suggests that there is no such severe shortage, even with twin pregnancies, where the greater competition might show itself in individual loss of birth-weight. Up till this week (beginning Monday, November 24, 1941) there has been a reasonable supply of milk, so that the mother has had at least 2 pints of milk available. This week there has been a cut in the ration so that, allowing for the shortage of milk and difficulties of distribution, the minimal ration for a pregnant woman of 1 pint per day will be the maximum for many pregnant women throughout the country. Allowing that in addition to the rationed foodstuffs she has weekly 3 lb. of cabbage, 7 lb. of brown bread, 2 lb. of carrots and 4 lb. of potatoes, there is evidence the protein intake and the vitamins A and B, are borderline. There is reason to suppose the daily ration of calories will not exceed 2,400, of calcium 1·3 mg., of iron 14 mg. per day, of vitamin D 70 I.U. and of ascorbic acid 90 mg. All these last five are in varying degree below the generally accepted minimal requirements. The calcium deficiency can be compensated in some degree after birth as also can the ascorbic acid; but this does not apply to iron. It is probable, therefore, that there may occur neonatal signs of malnutrition, notably hypochromic anæmia, infections and chest troubles, and possibly poor musculature.

Section of Anæsthetics

President—A. D. Marston, M.R.C.S., L.R.C.P., D.A.

[*November* 7, 1941]

The Centenary of the First Anæsthetic Use of Ether

PRESIDENT'S ADDRESS

By A. D. Marston, M.R.C.S., L.R.C.P., D.A.

As the centenary of the first anæsthetic use of ether occurs during the present session, I have taken this event as the subject of my Presidential Address, and will begin by a brief survey of the happenings of the Autumn of 1841 and the Spring of 1842.

Ether had been known for many years, and, according to Dudley Buxton [1], was discovered in 1540 by Valerius Cordus, who described it as "oleum vitrioli dulce". During the last quarter of the eighteenth century ether was employed medicinally for a number of diseases, amongst others, curiously enough, asthma and pulmonary tubercle, while at the time our story opens it had been increasingly used as an alternative to nitrous oxide gas for the production of the "frolics". These "frolics" were the strange parties in vogue at that time. They seem to have occurred only in Great Britain and America, and it is interesting to note that a French writer, M. Filvée, in his "Lettres sur l'Angleterre", published in 1802, described them as a vice peculiar to these countries, and an example of the increasing decadence of the Anglo-Saxon race. From these "frolics" the participants secured a thrill and much amusement, and in the Autumn of 1841 Crawford Williamson Long, a young physician practising in the obscure little town of Jefferson in the State of Georgia, U.S.A., gave a series of such parties at his house. At first he used nitrous oxide, but supplies of this were difficult to get, and so he used ether which he obtained from a local chemist named Goodman.

A studious brain and an observant eye were the fortunate possessions of Crawford Long, and he noticed that although bruises and minor injuries resulted from the tumbles and the reelings of the participants of the "frolics", neither they nor he himself suffered any immediate pain. Such a deduction led to the epic discovery of ether as an anæsthetic, and on March 30, 1842, Long administered ether to a young man named James M. Venable for the operation of removing a cyst from the occipito-cervical region. The administration of ether, which was performed before witnesses, was the simple inhalation of ether from a towel, and it was very successful. The patient was delighted at the complete absence of pain, and Crawford Long realized that he had made a great discovery. It needed courage on Long's part—more courage than is generally appreciated—to perform this operation on Venable without parental consent and against the advice of his friends. Here is an account from the writing of Mr. Jim Vandiver:

"The day that James Venable had a tumor cut out, I happened to be in Jefferson. I well remember it; can never forget that memorable day—March 30th, 1842. A group of excited men were gathered on the public square of the village not far from the little office of Dr. Long. I enquired the cause of this gathering and was told that Venable, in opposition to the wishes of his family, was letting Dr. Long put him to sleep to cut out a tumor. They vowed that should the boy fail to arouse from the effects of the ether, they would lynch Long. I did not see the operation, but I did station myself at the steps of the office in which the operation was being done, to beg the crowd to stand back and quietly await the result.

"Dr. Long was my friend and I believed in him. Not long to wait: the door opened, and we were told all was over. James Venable was safe and all right, the tumor out and no pain felt by the patient, the tumor in the possession of the miracle man". [2]

Read by Mrs. Eugenia Long Harper of Atlanta, Georgia before "The Circle"—Hon. Students' Society of the Marguette University School of Medicine—on April 30, 1934.)

Crawford Long operated on Venable for a second tumour on June 6 of the same year, and this undertaking proved almost as successful. On this occasion, however, Long only induced anæsthesia with ether, and then proceeded with the operation. This resulted in the anæsthesia becoming exceedingly light towards the end of the operation, which was probably concluded in a state of analgesia, because Venable noted that something was being done to him although it was not painful.

Long deduced from this that continuous inhalation of ether was probably necessary. This technique he observed in his next operation performed on July 3, 1842, for the amputation of a toe.

Subsequent operations were undertaken by Long with the help of ether on September 9, 1843, for the removal of a tumour from the head of Mary Vincent, of Jackson, and on January 8, 1845, for the amputation of a finger of a negro boy, the property of Ralph Bailey, Esqr., of Jackson, Georgia.

In 1844, nearly three years after Long's first anæsthetic, Horace Wells, a dentist of Hartford, Connecticut, started his pioneer work with nitrous oxide. Wells experimented with ether, but observing the choking sensation resulting from ether inhalation, decided to continue his anæsthetic work with nitrous oxide alone. As is well known, Horace Wells became insane, and according to Dudley Buxton "died in prison, by his own hand, having inhaled ether to secure euthanasia" [3]. Although he made no claim himself for the discovery of ether, his relatives and friends did so after his death.

To William T. G. Morton, a dentist of Boston, a pupil and sometime partner of Wells, must be given the distinction of conducting the first successful public demonstration of ether anæsthesia, which took place at the Massachusetts General Hospital on October 16, 1846. Although responsible for the practical application of ether as an anæsthetic, it seems that the agent was suggested to him by one of his teachers, Dr. Charles T. Jackson, of Boston.

Morton deserved great praise for his painstaking experiments with ether. He used to anæsthetize his pet dog, and he also placed himself under the influence of ether. In September 1846 he succeeded in putting himself to sleep for eight minutes whilst sitting in his dental chair. On recovering consciousness, he was much elated, and decided to extract a tooth under ether as soon as possible from a human patient. This he was quickly enabled to do, for a few minutes later his surgery bell rang, and Mr. Eben Frost was ushered in suffering from toothache and a swollen face. Mr. Frost requested Morton to mesmerize him for the extraction, but Morton said "No! I have something much better", and proceeded to give ether. It is recorded that "to the joy of the operator and the astonishment of the patient, the attempt was perfectly successful" [4].

After the Massachusetts demonstration, the use of ether quickly spread over the United States of America, but was hindered by the misguided attempt of Morton to patent ether as a compound known as "letheon". Morton also requested in 1849 that the Senate of the United States should give him a gratuity for his claim to be the discoverer of anæsthesia. This claim was vigorously contested by Jackson and the relatives of the late Horace Wells. This application, which was never granted, had at least one good result in bringing to light the undoubted claim of Crawford Long, who had independently discovered ether anæsthesia and, desiring neither notoriety nor reward, has received them from a grateful posterity.

About nine weeks after the Massachusetts demonstration, the elder Bigelow communicated with his old friend, Dr. Boott, in London, giving him details of his son's paper on the first use of ether. Thereupon, on Saturday, December 19, 1846, Mr. Robinson, a dental surgeon, administered ether and extracted teeth from a patient at the house of Dr. Boott in Gower Street, close to University College Hospital, in which institution on the following Monday, December 21, Mr. Liston amputated a leg, the ether being administered by Mr. Squire. An illustration of Squire's original ether inhaler may be seen in *Proc. Roy. Soc. Med.* (1930), **23**, 1130 (Sect. Anæsth., 48).

At this time, Dr. John Snow lived and practised medicine at 54, Frith Street, Soho, and was destined to become the first and possibly the most famous of British anæsthetists. It is just one hundred years since John Snow read his first scientific paper entitled "Asphyxia and on the Resuscitation of New-Born Children" before the Westminster Medical Society on October 16, 1841. Reading in the *Lancet* Bigelow's account

of the Massachusetts demonstration, Snow at once interested himself in the matter, and during the next few years accomplished two great feats of pioneer work. First, he noted the imperfect nature of the ether administration, and devised an inhaler (fig. 1). Secondly, he carried out a series of experiments which placed the pharmacology and physiological effects of ether on a scientific basis. These experiments were carried out on mice, birds, guinea-pigs and frogs, and were remarkable not only for their exactness but for the degree of clinical information they yielded.

As soon as Snow had perfected his ether inhaler, he obtained permission to use it in the dental out-patient department of St. George's Hospital, and this proved so successful that he was soon asked to attend on the in-patient operating days. A little later he was appointed to University College Hospital where he gave ether for Mr. Liston, one of the busiest and most brilliant surgeons of his day. John Snow soon built up a considerable private practice, and in the last ten years of his life administered about 450 anæsthetics per annum. He had the privilege of anæsthetizing Queen Victoria in the last two of her several confinements, and Her Majesty was graciously pleased to express

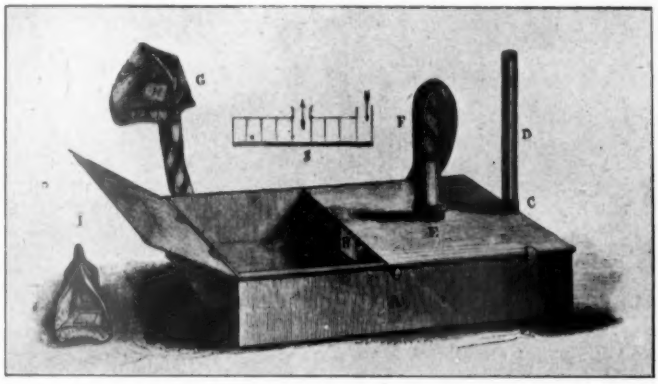


FIG. 1.—Snow's Ether Inhaler, 1847.

A. Box of japanned tin " the size and form of a thick octavo volume ". It served as a water bath. B. Ether chamber. C. Opening for filling and emptying. D. Tube for the ingress of air. The weight of air in the tube was intended to prevent evaporation into the room. E. To the opening E was screwed. F. A flexible tube about 3 ft. long. G. Facepiece. H. Inspiratory valve. I. Facepiece compressed to fit a smaller face. S. Section of ether chamber. [*From the Nuffield Department of Anæsthetics, Radcliffe Infirmary, Oxford.*]

her approval not only of the chloroform but also of the services of Dr. John Snow.

Most of Snow's work was with chloroform, but he always evinced great interest in ether. In his book he remarks:

" I prefer the flavour of ether vapour to that of chloroform, and the sensations I experience from the inhalation of ether are more pleasurable than those from chloroform " [5].

In Richardson's " Life of John Snow " we read:

" Once, he observed that in his opinion sulphuric ether was a safer narcotic than chloroform. Why, then, said a listener, do you not use ether? I use chloroform, he resumed, for the same reason that you use phosphorus matches instead of the tinderbox. An occasional risk never stands in the way of ready applicability " [6].

John Snow was a Yorkshire man, the eldest son of a farmer, and was born at York on June 15, 1813. He died on June 16, 1858, in his 45th year. He was attacked by his

fatal illness as he was writing the concluding sentence of his classic work on anæsthesia, which to this day remains famous and widely read (fig. 2).

Snow was aged 33 at the time he became an anæsthetic specialist, and he practised for only twelve years. Few men have accomplished so much original work in so short a time, and this is even more remarkable when one remembers that he was handicapped by poor health, and also that a good deal of his time was spent in research in subjects other than anæsthesia, including cholera and public sanitation.

Among those present at the first administration of ether at University College Hospital was a senior student named Joseph Clover (fig. 3), who was much interested in the proceedings. From that day until his death in 1882 he took an active part in the advance of anæsthesia. Joseph Clover was a Norfolk man and was born at Aylsham in 1825. His character has been described as gentle and amiable, and it has been written of him that "he was beloved by his patients and much respected by his medical colleagues". Clover was Resident Medical Officer of University College Hospital for five years, and during that period administered many anæsthetics. At this time Dr. Snow was probably the only anæsthetic specialist, and Clover was the first to follow his example. This choice of career was imposed upon Clover by his delicate constitution. In 1853 he became a Fellow of the Royal College of Surgeons, and showed great promise; but the hard life of a practising surgeon was too much for him, and so he decided to become an anæsthetist.

At this time the supremacy of chloroform, which, when introduced in 1847, became so popular as to supersede almost entirely the use of ether, began to wane on account of its dangers, and anæsthetists experimented with new methods to utilize the safer properties of ether.

The chief objections to ether were its slow and turbulent induction, and the difficulty of securing any steady level of maintenance anæsthesia. Apparatus was then primitive, and consisted in the use of a folded towel, a Rendle's cone, or a closed apparatus such as that of Squire, which entailed in the main re-breathing into a flask of two compartments, containing pieces of sponge and ether. All were unsatisfactory, and Clover's ether inhaler, which was produced after many experiments and much hard work, speedily displaced them. Various modifications were made from time to time, and this inhaler has been used by some anæsthetists right up to the present.

In 1864 the Royal Medical and Chirurgical Society of London, now the Royal Society of Medicine, appointed a committee to report upon the safety and efficiency of chloroform and ether. The committee, of which Clover was an advisory member, reported that ether was safer than chloroform, but that it was not an ideal method of anæsthesia because of its lengthy induction and the variable and uncertain character of its maintenance.

Clover described his completed apparatus in 1877. With it patients were induced comfortably with nitrous oxide gas, this being followed by ether and finally by ether vapour and air. By means of this apparatus, induction took from one and a half to two minutes, and afterwards it was possible to maintain a smooth anæsthesia for as long as might be required.

At about the same time as the introduction of Clover's inhaler, Dr. Ormsby, a Dublin physician, described his ether apparatus. Ormsby's inhaler was widely used and was preferred by some anæsthetists to that of Clover. Discussing the respective merits of the two inhalers, Sir Frederic Hewitt writes:

"For inducing anæsthesia by means of ether there is no apparatus which can be compared to that invented by Clover, for the anæsthetic vapour may be admitted so gradually that the initial discomforts are reduced to a minimum. But for maintaining ether anæsthesia Ormsby's inhaler is equal, and in many cases superior to Clover's. I have on several occasions changed from a Clover's to an Ormsby's inhaler with marked improvement in the symptoms of the patient. For example, I have often known cyanosis to quickly vanish and the breathing to become less hampered by effecting this change of inhalers during deep ether anæsthesia" [7].

This question of cyanosis with Clover's inhaler has always been its chief defect. Clover himself recognized this and invariably desired ether to be given with enough air to eliminate asphyxial symptoms. In later times this difficulty was finally solved by Lieutenant-Colonel Ashley Daly, who, as Nosworthy says: "employed the simple expedient of admitting sufficient oxygen through a tap in the angle-piece" [8].

I think it is correct to state that Clover's apparatus has been employed for ether

FIG. 2.—Autotype from a presentation portrait, 1856, and autograph facsimile. [*From the Nuffield Department of Anæsthetics, Radcliffe Infirmary, Oxford.*]

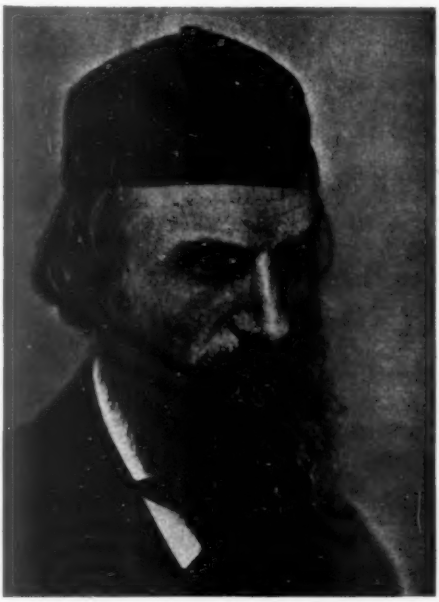


FIG. 3.—Joseph Thomas Clover (1825-1882). [*From a photographic portrait in the Nuffield Department of Anæsthetics, Radcliffe Infirmary, Oxford.*]

anæsthesia from its introduction in 1876 right up to the present time. But most anæsthetists abandoned its use in the last war when open ether or semi-open inhalation became popular. According to Rawdon-Smith: "The 'open' method was invented by L. H. Prince, of Berlin, U.S.A., and independently by Ferguson, of Boston. It was introduced into England in 1906 after the Toronto Meeting of the B.M.A." [9].

Gwathmey, in America, Shipway, Pembrey and Geoffrey Marshall, in England, did valuable work in directing attention to the advantages accruing from the suitable heating of ether vapour. Shipway's portable ether and chloroform apparatus had a considerable vogue and it was a useful and successful apparatus. "Mennell's bottles" were also largely used at this time, and were both simple and efficient.

About 1921, Pinson introduced his ether bomb, which was indeed an effective means of heating ether vapour, and it was the use of this apparatus which first led observers to query the advantage of heating ether vapour past a certain limit. Under the full anæsthesia obtained from Pinson's bomb, patients were sometimes observed to become flushed and actually to sweat. When much sweating occurred it was thought that more heat was perhaps thus lost than in the open administration of cold ether. On the Continent of Europe elaborate apparatus has been constructed such as the Tiegel-Henle-Sauerbruch and the Tiegel-Lauer, and these seem to have no advantage, for if ether is overheated it may well condense in the respiratory passages, with the production of harmful results.

As I have said, the epoch of ether warming had a definite vogue from 1915 until 1923, after which period most anæsthetists thought the matter had been overstressed and that the delivery of ether vapour at body or room temperature was the best.

In 1924, Langton Hewer wrote a paper entitled: "The Endo-tracheal Administration of Nitrous Oxide-Ethanesal as the Routine Anæsthetic of Choice for Major Surgery." In it he discussed the pros and cons of ether warming, and concluded by remarking: "As the result of these investigations the writer has now abandoned all extra heating" [10]. This paper was a valuable one because it also directed attention to the undoubted value of endotracheal administration of ether not only for the surgery of the face, lips, jaws and thorax, but also for major abdominal operations.

The subsequent development of ether administration by inhalation has been chiefly furthered by the work of Gwathmey, Guedel, Wesley Bourne, and Ralph Waters in the United States of America and in Canada, and by Boyle, Shipway, Rowbotham and Magill in this country.

Boyle's apparatus enabled ether to be used in a minimal capacity, that is, as an adjuvant to gas and oxygen. Boyle first introduced his apparatus in the Great War, and not excepting Clover's apparatus, it has probably had the greatest popularity of any anæsthetic apparatus. Boyle has been honoured for his work in anæsthetics both in this country and in America. He was an Honorary Member of our Section, and I am sure we are all very proud of the way in which he handed on the torch of progress in our special branch of medicine during the last generation.

In 1925, Webber introduced his modification of Boyle's bottles, which places the bottles in parallel instead of in series. In practice this arrangement works well and prevents any contamination of ether by previous transit of gas through the chloroform bottle.

RECTAL ETHER

Rectal ether (at first pure) was used by Pirogoff and Roux in 1847, but although this was found to be efficient as a mode of inducing anæsthesia, it was abandoned on account of the discomfort experienced by the patient and the damage caused to the local tissues.

Pirogoff later perfected an apparatus which warmed the ether and allowed only ether vapour to enter the rectum. This was more successful but was sometimes followed by unfortunate after-results such as meteorism, diarrhœa and melæna. No eminently satisfactory apparatus was produced in England until that of Dudley Buxton in about 1885. It was made for him by Messrs. Mayer and Meltzer, and in a personal communication Mr. Ernest Mayer says:

"The writer assisted Dr. Buxton at various operations at which this apparatus was used; once at King's College Hospital, Sir Joseph Lister being the operator, and on a brain case, Sir Victor Horsley being the surgeon."

This apparatus was a success, but Buxton in his description of "after-effects" quite honestly says:

"Colicky pains in the intestines, urgent tenesmus, diarrhœa, sometimes dysenteric in character, painful distention of the intestinal tract with more or less severe collapse are the complications which have been recorded."

and he concludes this rather dismal summary with these words: "Deaths have occurred" [11].

Dudley Buxton, M.D., was born in 1855 and died in 1931. He did an enormous amount of work in investigating the use and actions of ether, and encouraged its routine use instead of chloroform. In this he encountered opposition. He disagreed with the findings of the first Hyderabad Commission in 1889, and also of the second Commission held a little later on. A further service to ether administration was his rooted objection to any cyanosis. In this crusade also he met with opposition.

Buxton was a founder of the Society of Anæsthetists (in 1893) which later became the Anæsthetic Section of the Royal Society of Medicine. He was first appointed anæsthetist to Soho Square Hospital for Women, and afterwards to University College Hospital where he instituted systematic lectures on anæsthesia and introduced the custom of allowing students to administer anæsthetics under the supervision of a teacher.

The first Hyderabad Commission Report was reviewed by Dr. Buxton in the *Lancet*, and he pointed out that it was entirely inadequate and that the experiments were too few, were crudely conceived and were unscientifically carried out.

Conditions in the specialty of anæsthesia were indeed chaotic at the commencement of Buxton's career. We read that the status of the anæsthetist was almost negligible. For instance, if a surgeon needed a short anæsthetic to be given when examining a patient in his consulting room, the butler or footman would be called in to administer some nitrous oxide or a whiff of chloroform. In some hospitals the porters gave chloroform under the direction of the surgeon. Buxton is recorded as describing the occasion on which he was invited by a distinguished surgeon to meet the then President of the College of Physicians at a private house for the purpose of giving an anæsthetic for an examination. The surgeon conducted him upstairs, and, on opening the bedroom door, Buxton was amazed to find the physician and the patient rolling about the floor, locked in one another's arms. Not expecting an anæsthetist, the physician had attempted to start the anæsthetic, with—as Buxton observed—but indifferent success. Surely, argued Buxton, if so untoward an occurrence could happen under the auspices of such an august administrator, there was every reason for the existence of specialists in anæsthesia.

In 1913, Gwathmey introduced his ether-in-olive-oil technique, which was satisfactory and had a considerable popularity, specially in the Great War.

The chief use of rectal ether was to establish a method whereby operations could be successfully performed on the face, mouth, head, larynx and thorax. We seldom, if ever, hear of rectal ether to-day, partly because other agents such as avertin and paraldehyde given by the technique of Rowbotham have proved superior, but more particularly because it has been superseded by the development of the endotracheal method.

ENDOTRACHEAL ETHER INSUFFLATION

Kuhn (1900) and Elsberg of New York (1909) were the pioneers of this new method which was further developed by the work of Meltzer and Auer, and was first used in this country by Kelly of Liverpool in 1912. His apparatus is described in Minnitt's revised edition of Rose and Fairlie's "Handbook of Anæsthesia". It was modified and improved by Shipway in 1916.

Two advantages have been claimed for ether insufflation under positive pressure:

(1) The return flow of air issuing between the rigid gum-elastic catheter and the trachea was said to prevent the descent of any blood or oral secretion into the pulmonary alveoli, and experiments, which Kelly and other workers have performed on animals, have supported this theory. Clinical experience has, however, cast doubt upon this assertion, and Langton Hewer (*Brit. M. J.*, 1940 (i), 318) reported cases of tonsillectomy in which blood had actually been seen to gravitate along the catheter, and at the end of the operation was observed by bronchoscopy to have entered the lower respiratory system.

(2) The positive pressure of insufflation could be used to produce apnœa, so that the immobility of the chest might facilitate operative procedures in the upper abdomen

and thorax. Clinically, this practice was sometimes found to result in hypostatic congestion of the lungs.

I mention these claims to special advantage accruing from insufflation because protagonists of this technique have recently advocated it in preference to the type of endotrachael inhalation now in general use.

ENDOTRACHEAL INHALATION

This is low-pressured inhalation through a wide-bore soft rubber tube which fills (or nearly so) the trachea. This method was introduced by Rowbotham and Magill as the result of much experimental work performed in the plastic clinic at Sidcup during the Great War (1914-18).

In the opinion of most anæsthetists this method is more physiological than positive insufflation and produces fewer undesirable after-results. If used with ether, it enables the drug to be given in minimal quantities mixed with nitrous oxide and oxygen.

I must not conclude without a mention of Sir Frederic Hewitt and the great work he did with ether.

Sir Frederic Hewitt was born in London in 1857 and died in 1916 aged 59. He was educated at the Merchant Taylors School and Christ's College, Cambridge. He had a distinguished academic career at St. George's Hospital, winning several prizes, and graduated M.D. at Cambridge in 1884. He was made an M.V.O. in 1902 for his service as anæsthetist to King Edward VII, and was knighted in 1911. He did much to develop the use of ether, and his researches advanced our knowledge of its pharmacology.

Hewitt was originally a physician, and but for ill-health (he suffered from an incurable defect in his vision) would probably have practised as such. He did a great service to our specialty in elevating its status. This he accomplished by successfully persuading the examining bodies to include the subject of anæsthesia in the medical curriculum. He held strongly to the opinion that only qualified medical men should administer anæsthetics, and influenced the Home Office authorities to such a degree that a Bill for an Act of Parliament to this effect was actually introduced in the House of Lords in 1912. The congestion of legislation before the Great War, and the delay caused by a certain amount of opposition, prevented the matter from proceeding any further, however.

His textbook on anæsthesia, published in 1897, after ten years of careful and patient preparation, had reached its fifth edition at the time of his death in 1916. It has been described by Blomfield as "probably the best systematic exposition of the theory and practice of anæsthesia in any language" [12].

Hewitt was a man of great determination and courage. It is recorded that on one occasion, when confronted by a complete spasm of the glottis in the dental chair, he produced his penknife and coolly performed the operation of tracheotomy. This relieved the symptoms and the patient's life was saved.

It is interesting to note that as the centenary of ether approaches, new and valuable work has been carried out by Professor Macintosh and his co-workers in the Nuffield Research School at Oxford.

REFERENCES

1 BUXTON, DUDLEY (1900), "Anæsthetics: Their Uses and Administration", p. 98. 3rd Ed. London.
2 HARPER, EUGENIA LONG (1934), *Wisconsin M. J.*, **33**, 700.
3 BUXTON, DUDLEY (1900), "Anæsthetics: Their Uses and Administration", p. 7. 3rd Ed. London.
4 GWATHMEY, J. T. (1925), "Anæsthesia", p. 12. London.
5 SNOW, JOHN (1858), "On Chloroform and Other Anæsthetics", p. 357. London.
6 RICHARDSON, B. W. (1858), "The Life of John Snow, M.D.", p. 35. London.
7 HEWITT, Sir FREDERIC W. (1893), "Anæsthetics and Their Administration", p. 151. London.
8 NOSWORTHY, M. D. (1935), "The Theory and Practice of Anæsthesia", p. 72. London.
9 RAWDON-SMITH, G. F. (1926), "Dental Anæsthesia", p. 87. Edinburgh.
10 HEWER, C. LANGTON (1924), *Brit. J. Anæsth.*, **1**, 116.
11 BUXTON, DUDLEY (1900), "Anæsthetics: Their Uses and Administration", p. 139. 3rd Ed. London.
12 BLOMFIELD, J. (1926), *Brit. J. Anæsth.*, **3**, 122.

Section of Urology

President—G. E. NELIGAN, M.C., F.R.C.S.

[*November* 27, 1941]

DISCUSSION ON RUPTURE OF THE URETHRA AND ITS TREATMENT

Mr. Clifford Morson: Rupture of the urethra is the most serious of all injuries to the genito-urinary tract, not on account of the immediate mortality rate, which, *per se*, is negligible, but because of subsequent ill-health. I know of no case where the urethra has been completely torn across, in which the patient has been restored to perfect health. There may be a long interval between the date of injury and the onset of some lesion in the urinary tract directly attributable to the damage done to the urethra, but come it will. However, there are many ways of minimizing these dangers.

The causes of ruptured urethra are well known, but in view of the times we live in, one type of laceration of the urethral mucous membrane is of particular importance. Where there has been a comminuted fracture of the arch of the pubis due to a war wound, there is considerable danger that, subsequently, a spicule may be detached and penetrate the urethra. This complication may occur some years after the fracture has united. Thus in a case admitted to S. Peter's Hospital under my care, micturition had been normal ever since the pelvis had been fractured by a piece of shell during the 1914-18 war. Suddenly in 1925 this soldier was seized with pain in the perineum and retention of urine. The passage of a catheter was blocked by what was thought to be a stone, but X-rays demonstrated the presence of a small spicule of bone lying across and within the lumen of the membranous urethra. At operation it was found that this piece of bone had worked its way from the soft tissues adjacent to the arch of the pubis. Such a complication can obviously be prevented, when treating a gunshot wound of the pelvis, by removing all isolated fragments of bone. The site of the rupture can usually be determined by the nature of the injury. Blows of all kinds upon the perineum such as falls and kicks damage the posterior part of the bulbous urethra. This part is also involved when the penis itself is violently pulled on.

Crush injuries, causing fracture of the pelvis, affect the posterior urethra between the internal meatus and the triangular ligament. I have never met with a case of rupture of the urethra in the region of the compressor muscle.

The diagnosis of a rupture due to an accident or a gunshot wound is rarely difficult. If the urethra is completely torn across there will be retention of urine and escape of blood from the external meatus. Immediately following the injury there is an urge to micturate. An inability to carry out this act is a sure sign that the rupture of the urethra is complete. Many of the older textbooks teach that the patient must be told to hold his water. There is no need for this instruction. Micturition if at all possible will have taken place before the arrival of the doctor. If the rupture is incomplete a few drops of blood may appear at the external meatus followed by micturition in which the urine is blood-stained.

I am in entire agreement with the late Frank Kidd that on no account should a catheter be passed for diagnostic purposes. Damage to the mucous membrane is

thereby increased, the very thing which must be avoided. The more the tissues are torn the greater will be the formation of scar tissue. Bruising of the perineum indicates that there has been some degree of injury to the urethra, but the deciding factor in determining the extent of the injury is the ability of the patient to micturate. Frank Kidd stressed the value of the urethroscope. If there is any doubt at all as to whether the urethra is completely ruptured this is the only instrument which should be used. In every case of suspected injury to the urethra, the pelvis must be X-rayed, to exclude fracture. It is fortunate that this serious injury is unusual. Frank Kidd stated that out of a total of 14,000 in-patients admitted annually to the wards of the London Hospital there were only 4 cases of ruptured urethra. In ten years there were 41 (1909-1919). At the Whipps Cross Hospital from 1933-1938 there were 8 cases admitted out of an annual average admission of 17,000 patients. Obviously, in London at any rate, this accident is a rare one.

Treatment varies according to whether the rupture is complete or incomplete. If the latter it is only necessary to confine the patient to bed for a few days provided the pelvis is not fractured. Hæmaturia never persists for longer than a day or so. Instrumentation is entirely contra-indicated. Should a large hæmatoma form in the perineum it may be necessary to make a small incision over the swelling and remove the blood-clot. Most patients can be discharged within a week of the accident. Subsequently, urethroscopy is needed every six months to study the formation of scar tissue. At the end of a year it will be possible to determine by this method of investigation the degree of stricture formation, and how often dilatation will be required.

A study of the literature dealing with complete laceration of the urethra reveals many different opinions as to what should be done to the urethra itself, but every experienced urologist is agreed that as soon after the accident as possible the urine must be diverted. Delay is dangerous. A self-retaining angular tube of any of the well-known patterns must be inserted suprapubically into the bladder by the trocar and cannula technique.

The patient is severely shocked and, therefore, the tube should be inserted with a minimum of dissection. Painful sensations in the region of the bladder are never entirely abolished by anæsthesia infiltration; the anæsthesia of choice is either a spinal anæsthetic, or gas and oxygen, or pentothal.

No plastic operation should be performed on the urethra until primary and secondary shock have passed off, which may take from twenty-four to forty-eight hours. Therefore, about the third day, the surgeon can proceed, by whatever technique he favours, to join together the torn ends of the urethra. To delay longer will not only add to the difficulties of the operation but more scar tissue will have had time to form.

If the rupture is in the bulbous portion, the union of the torn ends is not particularly difficult.

A perineal dissection with the patient in the lithotomy position gives an excellent exposure. Union is accomplished with the finest plain catgut. The chromicized variety should not be used on account of its slow absorption. On no account should a catheter be tied in. Its presence causes irritation of the bruised mucous membrane, with a consequent increase in scar tissue at the site of the rupture. Suture material which is slow in absorption also produces the same result. It is my practice to leave a rubber wick as a drain, for forty-eight hours, in the peri-urethral tissues.

The suprapubic tube should be removed at the end of about a fortnight, or when the perineal wound has healed; and at the same time under gas-oxyen anæsthesia, a metal bougie, 10/12 Charrière size, is passed through the urethra into the bladder. This instrument must be used with the greatest gentleness.

The closure of the suprapubic fistula is always slow and does not occur until healing within the urethra is firmly established—a period of one or two months. During this time metal bougies should be passed once weekly. Unfortunately treatment does not end with the closure of the suprapubic fistula. The patient must be told that he will have a stricture for the rest of his life, and intermittent dilatation is necessary if serious complications are to be avoided at a later date. For the first year after this injury the dilatation has to be performed every six weeks, afterwards the intervals may be three to six months. Woe betide the patient if he ignores this advice. The gradual narrowing of the lumen of the urethra will produce all those changes in the bladder and upper urinary tract due to urethral obstruction which are so well known to all experienced urologists.

Laceration of the urethra at the junction of the prostatic and membranous portions

is an extremely serious injury, and attended by sequelæ which lead to permanent disabilities of the most distressing kind. Often the bladder is completely dislocated, so that there is a space between the internal meatus and the triangular ligament, the intervening portion of urethra having been crushed. In such cases the pelvis is always badly fractured. The initial treatment is the same as that of rupture of any other part of the urethra, namely immediate suprapubic cystotomy. Also, when the patient has recovered from the shock due to his injuries, an attempt must be made to repair the damage done to the urethra.

It must be admitted that ultimate results, no matter what technique is used, have been uniformly bad. In many cases the scarring is so extensive that micturition is impossible and the patient is condemned to a permanent cystotomy. In other cases the urine can be passed *per urethram* only if the stricture is dilated at frequent intervals, and this treatment supplemented by internal urethrotomy when the bougies fail to stretch the scar tissue. Often bladder sepsis is so severe that cystotomy becomes imperative. A recent experience with enucleation of an adenomatous prostate, so badly performed by one of my house surgeons that the bladder was torn completely away from its attachments to the pubis and its arches, suggests a technique which may produce better results than any of those already published. It is based on the modified Harris technique for prostatectomy and is briefly as follows:

With the patient in the Trendelenburg position the interior of the bladder is exposed in the usual way and flood-lit. The posterior lip of the torn internal meatus is picked up with a boomerang needle and stitched to the lacerated proximal end of the membranous urethra. The lateral margin of the mucous membrane of the internal meatus is then stitched to the superior surface of the triangular ligament on either side of the urethral opening. The insertion of a suprapubic angular tube completes the operation. With good illumination and skilful use of the boomerang needle this technique is not unduly difficult, but it presupposes the absence of the prostate. The whole of the prostatic urethra with the surrounding glandular tissue will have to be dissected away before it is possible to unite the internal meatus to the triangular ligament. The removal of the prostate may be criticized on the grounds that it will lead to sterility, but after the crushing of the urethra between the internal meatus and the triangular ligament, the patient is always sterile. Unfortunately the only case on which this technique was tried died from pneumonia a few weeks after the operation. The end-result, therefore, cannot be estimated.

The prognosis in rupture of the urethra is determined not so much by the character of the operation, as by the amount of scar tissue formed in and around the urethra.

Many of the factors controlling fibroblastic growth are well known, but others are surrounded by mystery.

In the case of the urethra, first, the position of the rupture plays an important part. Less scar tissue forms in the region of the anterior urethra than in the posterior position.

Second: the more extensive the laceration of mucous membrane, the worse is the stricture. At least we can avoid increasing the tear of this tissue by not jabbing at it with a catheter.

Third: the longer the delay in performing the plastic operation the more difficult it will be owing to development of granulation tissue. The latter consists chiefly of fibroblasts, the forerunners of scar tissue.

Fourth: the escape of urine into the tissues around the rupture will produce dense scarring. Here again we should be able to avoid this by performing cystotomy immediately after the accident. Thus it will be noted that though the surgeon cannot prevent complications at least it is within his power to control them.

Mr. Charles Wells: This subject is clearly defined by conventional classification into rupture of the external type in which the bulb is torn by direct violence, and the internal type in which the membrano-prostatic urethra is ruptured by indirect violence. To these may be added a small group of miscellaneous cases due to exceptional injuries.

In each group we have to consider problems of diagnosis, immediate treatment (both general and local), the prevention, occurrence and treatment of complications such as extravasation, the after-treatment and prognosis. We must then turn our attention to the late cases which are brought to our notice months or possibly years after the accident, having had either too much or too little, and almost certainly wrong, treatment in the

meantime. In this formidable programme, fortunately, the boundaries of the territory are clearly defined and the subdivisions sharply cut.

In external cases where the extent of the injury is in doubt, in which there is retention due to spasm and a little perineal bruising with some bleeding from the urethra, I attempt a rubber catheter and if it can be passed I leave it in position for a few days. Instrumentation should be carried out only with real aseptic precautions, preferably in the theatre where operation can be undertaken at once if necessary. How else is one to examine a doubtful case? The patient must not be allowed to micturate for fear of causing extravasation. If the passage of the catheter is at all difficult or impossible the bladder is opened with local anæsthesia. This is important, as under general anæsthesia the patient may void and extravasate. He is next anæsthetized and placed in a high lithotomy position. Instruments are passed in both directions and the urethra dissected out and sutured as a ribbon. A small rubber catheter (No. 4) is then drawn through as a guide to further instrumentation. The bladder is kept empty by the suprapubic route with an Ainsworth Davies metal tube attached to a suction pump. This keeps it empty and prevents urine from trickling down around the catheter into the perineal wound where it is the probable source of such infection, necrosis and, ultimately, the stricture commonly attributed to the catheter itself (Silverstone).

Similar suprapubic drainage with suction is part of the treatment in practically every case whether early or late.

One recent case of external rupture was reported to me by 'phone from a distance. Unable to go at once I advised a suprapubic cystotomy only, under local analgesia, and for various reasons a week elapsed before the urethra was explored. I then found a very large hæmatoma with wide separation of the ruptured ends. It is of some interest to report that this man made as good a recovery as any other, with as satisfactory an end-result. The lesson of this is clear—namely that, in the absence of extravasation, drainage will help the patient over and that thereafter there is no objection to waiting a few days for expert help in the perineal part of the operation. Deliberate postponement of repair has been advocated as a routine by Lepoutre. The danger of this course lies in the possible presence of undetected extravasation.

To the contrary, the undoing of a clumsy repair may take months of hard work. A second case illustrates this point. "M"—a soldier—sustained an external rupture early in 1939. I saw him for the first time at the beginning of this year. He had had at least two deliberate operations. There were stones in his right kidney with infection; cystitis with back pressure; and half a dozen fistulæ in his perineum, which were sodden and thickened. We drained him above the pubis and opened up all his fistulous tracks. After some weeks the stricture was excised and repaired and his urethra now functions well. In the meantime, however, stones had formed in his left kidney, and one became impacted in his ureter from which we removed it as an emergency. Weeks later he developed a peri-ureteric abscess which discharged spontaneously; and so on. The stones on the right side have still to be dealt with. All of this could have been avoided at the beginning.

Intrapelvic rupture through the membrano-prostatic zone may be missed and one should not be deceived by the finding of a little blood-stained urine upon catheterization. Once the diagnosis is made, operation with a view to reposition of the soft parts follows. By one means or another a catheter is threaded through from glans to bladder. My own practice is to stitch this firmly, with silkworm-gut, to a bladder tube. The prostate is then pushed down on to the triangular ligament and traction is made upon the catheter. It is undoubtedly desirable at this stage to reduce and fix the pelvic displacement which, having caused the rupture, is inevitably tending to hold the soft tissues apart. I believe that, as always, a well-planned and thoroughly completed operation is the surest road to a successful issue. In the case in point, every effort should be made to combine orthopædic with urological repair from the beginning. This is my view and I shall endeavour to put it into operation in future, even to the limit of immediate fixation in plaster which hitherto I have not done.

Late cases of internal rupture present some of the most engrossing problems. "S" was run over by a bus in 1927 at the age of 13. First seen ten years later, he had gross distortion of his pelvis and infantile external genitalia which had not grown since his accident. The bladder reached to the umbilicus and the ureters and kidneys were dilated to such a degree that one would have expected them to have ceased to function. He

wore a urinal day and night. The first essential was suprapubic drainage with slow decompression of the dilated upper urinary apparatus. Next we had to determine the extent of the damage. The bony distortion was apparent radiologically but urethrograms were disappointing. With double instrumentation under anæsthesia combined with rectal examination it was apparent that the prostate had risen high in the pelvis and that it was resting upon the upper surface of a large block of scar tissue uniting the separated pelvic bones. On the lower side of this huge scar was the under-developed bulbous and penile urethra.

The operation suggested by Watson in which the urethra is split so as to afford greater length was considered, but it did not promise sufficient urethra to meet the case from the atrophied bulbous portion, nor was there much prospect of finding anything at the prostatic end to which to suture it.

The perineum was duly opened up and a channel cut through the block of scar tissue so as to allow the shortest course between the separated ends, which were identified by passing bougies. The bulbous urethra was then dissected up freely but proved to be at least an inch too short. It was therefore split in its length so as to afford a flap, hinged at the blind end, sufficient to reach the bladder with ease.

The next difficulty was to find anything at the bladder end to which this urethral flap could be sutured. We eventually decided simply to anchor it in position and passed a catgut stitch through its extremity and drew this up through the prostate into the bladder. Finally this stitch was attached to the anterior abdominal wall by an intermediate length of elastic, thus affording continuous gentle traction. A fine catheter was put in as an aid to later instrumentation and the bladder drained by suction.

The subsequent history of this most difficult case was interesting. He micturated normally and attended irregularly for the passage of a small soft instrument which presented no difficulty. He worked at his job for rather more than two years after the operation and then died from an intercurrent acute infection of his irretrievably damaged urinary tract.

"J. J.", aged 9, was crushed by a heavy stone falling upon him. An early suprapubic drainage had saved his upper tract but left him with a grossly deficient urethra and a high prostate lying very close to the rectum. An operation, identical with the one just described, successfully reconstituted his urethra but the first subsequent instrumentation gave him a urethro-rectal fistula. An attempt to close this locally failed and we had resort to mobilization of the rectum as admirably described by H. H. Young. The muco-cutaneous junction at the anus is incised and the anal canal mobilized from within the anal sphincter. The bowel is then drawn down until the damaged portion is all outside, when the external part is cut off and the remainder re-sutured to the skin. This operation was a complete success but we still had difficulty in instrumentation because of a curious flap formation (the nature of which remained obscure) in the prostatic urethra. This was destroyed from the bladder aspect and since then all has been well.

In "L. M. J.", another small boy run over by a bus, the unsplit urethra was fixed with a similar transvesical anchor, the prostatic end being quite unsuitable for suturing. This is a most valuable manœuvre.

In all these cases, assiduous dilatation at regular intervals conduced to a happy result.

I do not wish to generalize from these particular cases except to emphasize (1) the advantages of suprapubic suction drainage and (2) the fact that with care a very little urethra can be made to go a very long way. In my opinion practically no case should ever be abandoned to permanent suprapubic drainage or converted to colonic implantation as has been suggested elsewhere.

BIBLIOGRAPHY

BAILEY, HAMILTON (1928), *Brit. J. Surg.*, **15**, 370.
Id. (1940), "Emergency Surgery", 4th Ed. Bristol.
DELZELL and STEVENS (1935), *J. Urol.*, **34**, 373.
HINMAN (1935), "Principles and Practice of Urology", 838. Philadelphia.
HUTCHINS (1938), *Am. J. Surg.*, **42**, 765.
KIDD (1921), *1er Congrés de la Soc. Internat. d'Urol.*, **1**, 169.
MARTIN (1935), *J. Urol.*, **34**, 718.
MCCREA (1940), "Diseases of the Urethra and Penis". Bristol.

MORRISON, R. (1916), " Surgical Contributions ". Bristol.
SILVERSTONE, M. (1941) (Liverpool. Personal communication).
SIMPSON-SMITH, A. (1930), *Brit. J. Surg.*, **24**, 309.
THOMSON-WALKER (1936), " Genito-Urinary Surgery ". 2nd Ed., 632. London.
WATSON (1935), *J. Urol.*, **33**, 64.
WELLS, CHARLES (1940), *Brit. J. Urol.*, **13**, 8.
YOUNG, H. H. (1929), *ibid.*, **21**, 417.

Mr. Hugh C. Barry: These cases belong to the realm of accident surgery and it is mainly the chronic cases and the failures that find their way to genito-urinary specialists. In no condition is it truer to say that prevention is more important than cure. Many of the tragedies are caused by mismanagement in the first few hours. Moreover it is important to realize that at this stage often other complications, e.g. hæmorrhage, shock and a fractured pelvis, may need treatment as well.

Because the condition is so rare no single method has had an extended trial and even now the casualty surgeon is faced with a number of conflicting views. Moreover because it is an inexperienced casualty surgeon and not a genito-urinary specialist who has to treat these cases first we must give preference to some simple and safe method of management, and if possible make it standardized. I would like to report three acute cases I have treated recently as they illustrate three distinct types, and, I regret to say, most of the complications that may arise.

CASE I.—K. T. S., a schoolboy aged 11, was climbing a fence when he slipped and fell astride. He had a painful swelling of his scrotum and was unable to pass water. There was no bleeding from the meatus when he was first examined. A soft rubber catheter was passed and withdrew clear urine. As there was now a little bleeding from the meatus it was tied in for twenty-four hours. Three days later he got acute retention and it was reinserted and left tied in. Nine days after the accident as his scrotum was still painful and urine was leaking around the catheter a suprapubic catheter was inserted and the urethral catheter removed. A week later I opened a periurethral abscess and found an inch of his urethra in a sloughing condition. Fortunately in spite of this large gap the perineal wound healed and after four months he was passing water normally. He will however require regular dilatation for the rest of his life.

This case illustrates some of the pitfalls of an indwelling catheter. Even the change from a perineal hæmatoma to an actual peri-urethral abscess was not as apparent to an unskilled observer as one might imagine. There was probably at first only a minute linear tear and I have no doubt that an immediate suprapubic cystotomy would have prevented this distressing result.

CASE II.—G. A., a man aged 32, was riding a motor cycle which skidded and crashed. He was able to walk home, but about an hour later noticed blood dripping from his urethra, and found he was unable to pass water. There was no evidence of bruising in the perineum. His lower abdomen was tender and dull on percussion, especially on the left side. There was no rigidity and intestinal sounds were present. A soft rubber catheter was passed and withdrew urine and a little dark altered blood. A subsequent X-ray showed a fracture of the left pubic ramus with very slight separation. A lower mid-line incision revealed an extravasation of blood in the prevesical space and an intact bladder. Suprapubic cystotomy was performed and a de Pezzer catheter tied in. The urethral catheter was withdrawn, and the prevesical space was drained. Three weeks later the urethra was dilated without difficulty and the de Pezzer catheter was removed. The suprapubic wound healed rapidly and he has remained well since, but is attending as an out-patient for regular dilatation. He has a stricture of the membranous urethra which though easily dilated has still a strong tendency to recur.

CASE III.—R. J. W., a schoolboy aged 7, was admitted to hospital, having been knocked down by a lorry. He was extremely shocked on admission (blood-pressure 68/40), showed signs of increasing pallor, and was obviously bleeding internally. There was a large bruise over the left costal margin, no bruising in the perineum and no bleeding from the urethra. The abdomen was tender, especially suprapubically, and no intestinal sounds were audible. X-ray showed slight separation of the symphysis pubis. A diagnosis of ruptured spleen was made.

An upper paramedian incision revealed a large extravasation of blood in the extraperitoneal tissues but no intraperitoneal lesion. On prolonging the incision downwards the bladder was found distended and dislocated backwards. A urethral catheter was passed and entered the prevesical space. Suprapubic cystotomy was performed and the hæmorrhage arising from the base of the bladder was controlled by packing. A blood transfusion commenced before the operation was continued after his return to the ward.

The boy recovered surprisingly well and two days later his wound was reopened and a urethral catheter was tied into the bladder. It was removed a month later, but he never regained control of his sphincter, and in spite of several dilatations a stricture soon developed. This led to an ascending infection and it has been necessary to dilate the suprapubic opening again and defer further instrumentation. He still is of course a long way from a happy result. The bruising of the costal margin was misleading but the case illustrates how severe hæmorrhage may be in this type of ruptured urethra.

I would like to submit the following simple rules for the emergency treatment of ruptured urethra.

ANTERIOR OR EXTRAPELVIC RUPTURE

The diagnosis is made if there is bruising in the perineum and bleeding from the external meatus. No catheter should be passed.

If the patient passes a normal stream of urine no special treatment is necessary at this stage, but he should be kept under observation, and his urethra should be examined after three weeks.

If there is any difficulty an immediate suprapubic cystotomy is performed to short-circuit the urine.

When there is a large perineal hæmatoma present it is incised and the urethra exposed. If the lesion is a complete rupture the proximal end is identified by passing a retrograde catheter and the roof is united by a few interrupted stitches. The wound is left open. The perineal incision and suture of the urethra are not essential at this stage and may well be left for a week and to a more experienced surgeon. Suprapubic drainage must never be neglected.

POSTERIOR OR INTRAPELVIC RUPTURE

If necessary a catheter may be passed to clinch the diagnosis. Unless a normal quantity of clear urine is obtained the diagnosis of rupture of the urethra or bladder is made. Accessory investigations are unnecessary and may be misleading. If the patient's condition permits it, the pelvis is X-rayed.

Immediate suprapubic cystotomy is performed, preferably under local anæsthesia when the patient is shocked.

If the lesion is incomplete a self-retaining suprapubic catheter is left in and the prevesical space is drained.

If the lesion is complete (i.e. when the base of the bladder is dislocated), the anatomy of the soft parts should be restored at once. A urethral bougie is passed till it just emerges through the membranous sphincter. A finger is then placed in the internal meatus and it is pushed down till the bougie can be made to enter the bladder. A self-retaining urethral catheter is then withdrawn. If the bladder still tends to redisplace, a rubber cuff is fitted to the catheter and continuous traction maintained. This type of rupture is the only one where an indwelling urethral catheter is indicated as well as suprapubic drainage.

All cases should be examined, preferably by a genito-urinary surgeon, within three weeks and regular dilatation commenced.

Finally it may not be too irrelevant to refer to the practice of "subincision" among the Australian aboriginals. It is their custom to incise the urethra from below, and in many of the elderly men the incision extends from the external meatus to the scrotum. While studying water metabolism with a Sydney University expedition in Central Australia I often had to collect twenty-four-hourly specimens of urine from these men. I cannot remember any strictures and one is tempted to conclude that this was because doctors were very scarce and catheters were unknown.

Mr. E. W. Riches thought that the opening speakers had done well to raise so many controversial points. On the question of suprapubic drainage there seemed to be a general agreement that it was desirable. There was some difference of opinion about a perineal incision in bulbar ruptures; in many of the cases mentioned in the discussion or quoted in the literature such an incision had become necessary later because of abscess formation or extravasation, and he considered that in most cases it should not be deferred. Immediate or delayed repair was another debatable question; it must be decided by the general condition of the patient and the amount of local trauma. Whilst immediate repair was the theoretical ideal, delay might be dictated by a condition of extreme shock, but such delay should be minimal, especially in intrapelvic ruptures.

The use of an indwelling catheter provided the greatest bone of contention; it appeared to him that if stricture was inevitable, as was suggested by most speakers, the objections to an indwelling catheter lost most of their validity. In a case of intrapelvic rupture with dislocation of the bladder such a means provided the simplest method of accurate repair, and whilst the operation suggested by Mr. Morson was ingenious he thought that reposition around a catheter would probably achieve the same result with less disturbance.

He agreed with Mr. Morson on the value of internal urethrotomy in some of the late cases of stricture. He quoted a case where a large renal calculus of the "recumbency" type had developed within a year of a urethral rupture for which the patient had been in bed for six months.

Mr. R. L. Benison: I am surprised by Mr. Morson's advocacy of urethroscopy for the diagnosis of acute urethral injuries, and think that the urethroscope is possessed of all the disadvantages of a catheter, with the additional possibility of air embolism. In dealing with injuries of the posterior urethra, there is a danger of waiting too long before undertaking operation, as the injury itself is aggravating shock all the time until it is properly dealt with. I think that eight hours is about the maximum time one ought to wait. I have found that the introduction of a small-sized self-retaining catheter, with a sound in the anterior urethra and a forefinger in the internal urinary meatus, is the easiest method of dealing with these injuries.

Mr. Morson in answer to Mr. Benison's remarks pointed out that the technique of urethroscopy was totally different from that of catheterization. Thousands of urethroscopies were performed every year in this country and it was rarely that a case of so-called air embolism was reported. When a death occurred during urethroscopy post-mortem always showed cardiac degeneration.

Section of Neurology

President—GEORGE RIDDOCH, M.D.

[*December* 18, 1941]

DISCUSSION ON REHABILITATION AFTER INJURIES TO THE CENTRAL NERVOUS SYSTEM

Professor Geoffrey Jefferson (*in absentia. Read by Colonel Riddoch*): In peace-time most doctors were fully aware that a problem existed in the after-care of those who had suffered a head injury. It was a problem that interested not only the neurological fraternity who saw only a fraction of the cases that existed in the country as a whole, for it was not then, nor is it now, a matter in which any single type of specialist is concerned. The general practitioner is deeply interested, or at least heavily involved, and has a vital part to play. If we disagree sometimes with what he teaches his patients we have ourselves to blame for our teaching to him and, more generally, for our acquiescence with a state of affairs that has vaguely troubled our consciences without our becoming sufficiently aroused to excite concerted action. In civil hospital practice there have been great difficulties (and I fear that they will for some time continue) in pursuing a more rational policy, the chief being the lack of control over the conduct and welfare of his patient once he leaves hospital. One chief difficulty has been the deficiency in bed accommodation in first-class hospitals in which the patient might have been kept until his first stage of convalescence was completed. This has led to the patient rehabilitating himself as best he could under his doctor's supervision. And in an industrial population, which has formed the major part of my own material, this has proved to be a slow process, how slow the following figures testify. I looked up a consecutive series of 50 head injuries seen in private practice during the last two years to find out how soon these cases had been referred for specialist advice for the first time: The average time was six months (from three weeks to two years). Many were not seen until seven, eight or nine months or more after injury. By that time a neurosis had become firmly established in a number of the cases, and few were within measurable distance of returning to their work, although most were free from organic nervous defects. The worst offenders are the Insurance Companies, who allow the cases to drag on inconclusively for long periods, before asking advice from a neurological specialist. It is rarely that a case is settled in the High Court or Assize Courts in less than a year.

As to the validity of all headache after a head injury there are many honest doubters (and be it admitted, we have doubts ourselves). We are learning steadily about the mechanism of headache and are abandoning some time-honoured creeds, notably the relationships between pressure and headache as against local distortions of dural septa and traction on, or pulsation of, vessels. We do not yet know with certainty how to apply this knowledge to those with head injuries, except that we have comparative knowledge that pain that continues with unwavering intensity for months on end rarely has an organic cause. But we appear to be at length on the right lines. Attractive as the "unresolved contusion" of Trotter was, it seems unlikely to survive critical scrutiny either as an entity in itself or, it follows, as a cause of persistent pain. I must avoid speaking too much about the well-known post-contusional syndrome, and we must beware, also, of the danger of coming to regard all who have had a head injury as neurotics, though it would not be far wrong to regard all of them, as I believe that we do, as potential neurotics. Too rigid a belief in such a generalization would place the post-traumatic invalids under the shadow of suspicion and medico-legal abuse from which Trotter did so much to rescue them.

What plan can we evolve to rationalize the treatment of these cases, what can we do to improve the lot of those with head injuries? Anything that we, as a profession, do must have as its first aim the benefit of the patient. I do not think that we need have any qualms of conscience on that point. Rehabilitation serves the patient primarily; it protects the social fabric indirectly. I mean that we are not sacrificing him to the needs of the State, and my experience of our own people is that they are resisting sacrifices at any such altar. Gross abuses have occurred in the past, but they have been wholly in the patients' favour; they are likely to occur again if we find ourselves unable to agree upon a plan and to act accordingly. There is first, the treatment of the patient himself; second, the bringing in of the general practitioner and regimental or unit officers; thirdly, the re-education of the general public which makes up the patient's family, his friends, his employers, his lawyers, and his judges.

Rehabilitation of the patient: after head injury.—Rehabilitation may be defined as: "The planned attempt under skilled direction by the use of all available measures to restore or improve the health, usefulness and happiness of those who have suffered an injury, or are recovering from a disease. Its further object is to return them to the service of the community in the shortest time." Although it is a new word, rehabilitation is an old purpose. All medical treatment has basically no other aim. In the early stages of hospital treatment the ministrations and supervision of the physician and surgeon, with their staffs, is to the forefront. It was well recognized in peace-time practice that the discharge of the patient did not denote the end of treatment and by the use of convalescent homes, out-patient follow-ups, and especially by the co-operation of lady almoners, a basis for subsequent supervision was present. It was, however, most used for the purpose of scientific follow-up, much less with the object of placing the patient back in work, and so was imperfect. It would be untrue to say that rehabilitation in the sense in which the term is now used would start only at the point where ordinary in-patient treatment ends, for it should have begun before. But it begins especially at the convalescent stage if we speak of measures which our hospital system has, except in special instances, hitherto lacked. And, what is more, it is carried on until the patient returns to work. It is a continuum closely interwoven throughout with the general medical care of the patient. It is a work in which all can help, and does not fall within the ambit of any one man or of any one speciality. It is planned so as to give the patient a sense of his own importance as an integral part of the social structure, to give him not only physical but mental employment day by day, and throughout the day to ensure a sense of accomplishment, of achievement. It gives him the opportunity to discover that he is, however much he is damaged, an individual with powers that he can still usefully employ. It affords him the chance of discovering that his wage-earning capacity is not lost and it should allow him to turn to other trades or means of livelihood more fitted to his powers, if that be necessary. Rehabilitation has hitherto been applied only sporadically and there are great inequalities. Indeed, as a national and planned effort rehabilitation cannot as yet be said to exist and the present fluid state of the hospital system makes it a favourable time for an experimental beginning on a reasonably wide scale. These measures should be regarded as an essential part of treatment and should be commenced, in a graded way, *as soon as the patient's condition allows.* Thus, occupation in bed and in the ward is as important as occupation elsewhere for the ambulant patient. In this way the boredom, laziness and loss of adaptability, so often acquired during a prolonged stay in hospital, will be prevented. From the first the patient must be made to realize that he is an active collaborator in his own treatment and that he must accept some responsibility in his progress towards a successful result. At this point it would be as well to emphasize the need for discipline in the E.M.S. Hospitals which varies not only from one centre to another, but from ward to ward in the same place. Complaints about indiscipline reflect on the hospital as a whole.

We do not advocate the imposition of dictatorial rule, believing that co-operation of the patient can be achieved by explanation and reasoning and that habits of tidiness and punctuality can be inculcated without hardship and by example. This is an essential principle in treatment and applies to the relationship between doctor and patient in all hospitals, whether E.M.S. or not. The methods to be employed in such treatment should include:

(1) *Diversional and also constructive occupations* of sufficient variety and varying degrees of difficulty for those still confined to bed, as well as for those who are ambulant.

(2) *Hospital maintenance work* in the ward and outside.
(3) *Physiotherapy*, remedial exercises, massage, physical training.
(4) *Intellectual and recreational pursuits.*

STAGES IN REHABILITATION

Rehabilitation may be divided up into stages corresponding with the progress of the patient from his original admission to hospital, through to his discharge and back to his home and employment.

Stage I

This covers the period during which the patient is in hospital—confined to bed or ambulant and is undergoing the early treatment appropriate to the local repair of his injury. Both Service and civilian casualties are included in this period under the agreement by which the E.M.S. cares for the injured, whatever their employment. In this stage the actual time at which the patient's interest is specifically aroused cannot be laid down definitely, because it will vary with the severity of the injury, the speed of recovery, the patient's age and intelligence, and the degree in which mental alertness and ability to co-operate have been depressed by the injury. But it should be laid down that rehabilitation in a diversional form should be instituted early whilst the patient is confined to bed. It will take the form of: Reading or being read to; jig-saw, cross-word, and other puzzles; drawing or colouring; needlework, string net and basket making; sewing, knitting, rug-making.

Speech therapy.—The retraining of speech by a Speech Therapist will be required in most cases of dysphasia. This treatment should be started when convalescence is well established, about the third or fourth week. For ambulant patients and those in wheel-chairs rehabilitation will be continued by book-binding; string and basket work; leather and metal work; simple carpentry, &c. Entertainments by concerts and films and, for the walking cases dancing is already available in some Brain Injury Centres. Patients after head injuries are often disturbed by noise and especially by general conversation. They may become distressed in a room where a gramophone is playing and other people are talking or playing games. A silence room of fair size and attractiveness should be set aside for them.

One of the most important services which rehabilitation will perform is that by instituting occupation to a time-table, the patient's day, or a considerable part of it, is dedicated to some pursuit. Clearly all such arrangements must be suited to the clinical state of the individual and the time-table will be most applicable to those advancing well in their convalescence. No doctrinaire rigidity is intended in any of the suggestions here advanced, which are to be applied with insight and judgment and modified from day to day, as needs be.

The scheme of rehabilitation above outlined refers to the patient with an uncomplicated head injury. If serious injuries exist elsewhere they might predominate and necessitate such modification of the plan as common sense dictates.

Physiotherapy will be required (it has of course already been provided in all the Brain Injury Centres). Physiotherapy should not dominate the general rehabilitation scheme which is a co-operative affair in which all branches play a helpful part. Undue emphasis has come to be laid on physiotherapy (massage, medical electricity in its various forms, and remedial gymnastics) because it has been the only kind of treatment commonly provided hitherto. Our hospitals, whilst well equipped for these treatments have lacked any organization for other convalescent pursuits, especially those that retrained the mind and took account of the personality and idiosyncrasies of the patients. It is our belief that of the two kinds of treatment, mental occupation and encouragement to do things, to make things, to use the whole body, is much the more important. Physiotherapy occupies a very small part of the patient's day and, except for remedial exercises, does not demand his co-operation. He is free for the rest of the day to follow the path of least resistance so that he tends to become the passive recipient of occasional treatment, dependent on others to get him well. However skilful physiotherapy may be, and it is commonly technically very skilful, many patients (not surprisingly) make slow progress.

The patient convalescent from head injuries is something very different. He should be urged to use his mind and to take an active part in his treatment, which will, without his interested co-operation, surely fail. With the other types of occupation included in rehabilitation there are things which excite interest over many hours of the day. In

several, e.g. where things are made with the hands, the important stimuli of competition and mimicry come into play, whilst in his constructive attempts he makes those very movements of his own with which physiotherapy teaches him for such short times and at intervals.

That the benefit of physiotherapy is often chiefly psychological cannot be denied, but this very fact calls for its intelligent use and the avoidance of misuse. During that stage of rehabilitation which coincides with the earliest stages of recovery, massage and encouragement to move paretic limbs will be the chief function of physiotherapy. Electrical methods are not advisable in the upper neuron lesions which form practically the whole of the material—the only exceptions will be the occasional facial nerve injuries and injuries to a limb or to peripheral nerves.

Stage I will last for about six weeks. This time might have to be extended in patients with chronic infections, cerebral fungus and the like, and those needing extended speech retraining. Modern surgical methods, and especially the new antiseptics give us grounds for the belief that long residence in hospital for purely surgical reasons connected with the wound will be uncommon.

The place of psychology in rehabilitation.—A bold statement on this question is necessary, and my belief is this that the proper use of the psychologist is that he should give reports on cases of head injury in much the same way that reports are given by other specialists, such as the radiologist and pathologist.

Whilst it is often instructive to know the intelligence quotient of a patient, it is more important for our purpose to assess his character, his emotional qualities, his recognition of values, his reactions to problems, his aims in life.

In the more serious injuries, where some degree of traumatic dementia has occurred, the psychiatrist's experience will fortify us in estimating the degree of mental damage.

Stage II

After some six weeks have elapsed since the injury we should be in a position to gauge the prospects of a case. Judged by experience from neuro-surgical operations, where variable degrees of considered and carefully inflicted damage is done to the brain, we know that in some six to eight weeks the effects of the operation have passed away. Reflections of this kind are important. Who can doubt that the two to three week period of invalidism that follows a section of the trigeminal root for neuralgia, or the slightly longer period after an operation for a pituitary adenoma, would be enormously extended in time were it the result of accident. Most scars are healed in two months, and after that period has elapsed the pain of a fractured skull (and I believe that most clinicians underrate bone pain) should have faded away.

Once symptoms have abated, the second stage or period of hardening commences. It seems desirable that military cases should be taken over by the respective Services for this purpose, since this gives an opportunity for canalization towards the specific goal of their line of work, whichever it may be. I shall leave discussion of the management of Service cases to the proper authorities. I will, however, outline the types of activity which are useful once the patient is fully ambulant and relatively free from complaints.

It is at this point, when daily medical and surgical supervision is no longer needed, that we advise separation of the military or Service casualties from the civilian, and it is here that the chief reconstruction and replanning between the E.M.S. and the Services will be advisable. Service patients recoverable for Service purposes ought to be rehabilitated in Service Depots under discipline and in Service pursuits.

Invalided Service and civilian patients.—The methods of treatment to be employed will be, in the main, the same as in Stage I, but with additions such as: (1) Gymnastics and physical training. (2) Continuation of physiotherapy when necessary. (3) Basket making, leather and metal work, the patient being allowed to keep the finished article on paying the cost of materials. (4) Speech-training for those with dysphasias. (5) Work in the garden. (6) Work in the carpenter's and engineer's shops. (7) Organized games—cricket, football, netball, baseball, rounders, and open-air games. (8) Walks outside the hospital grounds. (9) Visits to the town, shops and cinema, but usually with the purpose of finding out how the patient reacts to the jostle of people and the noise of traffic, to navigating himself as an entity amongst his fellow men. The same of visits to the cinema —how well does he sustain visual and auditory attention over a period of two hours or so and is he upset by the incidental noise? No patient with a head injury should go on

a bus or train journey until he has proved his ability to look after himself in this way.

It is not intended that these visits should be purely educational or therapeutic, but it is important that the doctors, in whose charge the patients are, should realize the lessons to be learned from these extramural activities. The patients must therefore be questioned about their reactions to these excursions, and progress notes made.

Physiotherapy will be applied where it is needed. The recreational side, such as attendance at dances, will be more in evidence.

An essential of rehabilitation is that it should be planned to a time-table each day. Patients should continue with a pastime or constructive work only for definite periods; he should be stopped whilst he still wishes to go on. In that way interest is maintained. Hence application at any one thing should be relatively short, especially in the earlier days of convalescence. The best plan will be to arrange 6 sessions for each patient in the day, of from forty-five to sixty minutes each, say from 9 to 12 and from 1.30 to 4.30. Everyone should be told his duties for the week with, say, Wednesday and Saturday afternoons free.

After six weeks or so in hospital with plenty of interest during Stage I he might feel himself quite well enough to return to home and to work without further preparation. It may be objected that patients will be reluctant to continue with further treatment, preferring to go home. The confidence of the patient in his treatment and the enthusiasm with which his doctors are able to advocate a continuation will determine his willingness.

The most important stage of rehabilitation is the first. The patient should be frankly told what sort of an injury he has had and what we expect the course of it will be. A great deal of our difficulties in the past have arisen because we have not been able to retain our head injury cases for long enough. Much can be done by giving the patient's doctor not only the history of the case, but also warning him against the possibility of the patient becoming a passive resister to cure. The mental resources of many of the industrial population are so few that the wonder is how they fill in the weeks and months and sometimes years that they spend in recovering. We can do much by establishing contact with the general practitioner and his counterpart in the Army, the Regimental Medical Officer. Further, by speech with the wife or relatives of the patient we can make them aware of the most important facts about head injuries and their course and can divert them from a degree of over-solicitude.

Professor Hugh Cairns: In any discussion on rehabilitation of head injury patients it is important to consider the main factors which influence the patients' disability.

(1) *The time factor.*—The time factor varies greatly from case to case. After a head injury the patient goes through a cycle, beginning with unconsciousness, thence through a stage of confusion and a period in which he is liable to headaches, to a final stage in which he is restored to normal or near-normal. This is a spontaneous process. The time taken for its completion may be in one case only a few weeks, in another as long as eighteen months, depending to a large extent upon the severity of the initial injury.

This time factor must always be taken into account in planning the rehabilitation of head injury patients, the more so because we do not yet possess adequate tests by which to measure the recovery of the higher levels of intellectual function. A man may appear on testing to have recovered his faculties completely, and yet he will fail on the intellectual level when he returns to his work. In deciding when a patient should be fit to return to work it is therefore necessary to bear in mind the severity of his injury, and the best yardstick at present available is the duration of the post-traumatic amnesia (P.T.A.). As a working rule I would suggest that the shortest time in which ability to carry out full work may be expected to return is as follows:

P.T.A. 5 minutes—1 hour	4—6 weeks
P.T.A. 1—24 hours	6—8 weeks
P.T.A. 1—7 days	2—4 months
P.T.A. over 7 days	4—8 months

I put this forward tentatively as a rough measure to be used in planning rehabilitation. It can be no more than a rough working guide because the duration of post-traumatic amnesia is influenced by other events besides the severity of the brain injury, e.g. the amount of bodily fatigue present at the time of injury, large doses of morphia or a general anæsthetic shortly after the injury, epileptic seizures in the first days after injury, and various psychoneurotic factors. Furthermore, we know that in certain cases where

there is a fracture of the base of the skull and the amnesia is shortlived, damage to the cranial nerves may interfere with return to work long after the higher cerebral functions have recovered. The type of work must also be taken into account; a simple task may be resumed earlier than one which involves the higher levels of intellectual function.

(2) *Disturbance of mental capacity.*—The central disturbance, the main organic cause of disability after head injury, is disturbance of mental capacity. It may occur at various levels of mental activity. At the lower levels there may be disturbance of speech, reading, calculating, or orientation. Initiative, memory and concentration may be affected. At higher levels there may be impairment of judgment, or of the capacity for abstract reasoning. The patient cannot be satisfactorily guided through the stages of rehabilitation without an attempt on the part of the doctor—however halting it may still be—to assess his mind in terms of these functions. After severe head injury the question will arise whether the patient is likely to be fit for his previous work, and this will often largely depend upon his retention of the capacity to learn. While the patient continues to show improvement an adverse decision should usually be withheld.

(3) *Emotional disturbance.*—Emotional factors are inextricably bound up with the process of recovery. The unstable type of man will have additional difficulties in adjusting himself to the task of returning to work, and it is therefore incumbent on those responsible for rehabilitation to assess the man as well as the severity of his injury. This is best done not only by observing the patient's behaviour while under observation, but also by a systematic inquiry into his family history, and into his earlier life and illnesses. The doctor may learn, especially in the cases of soldiers in war time, that before his accident the man was not employed, or felt that he was not employed, in the type of work for which he was best fitted.

Emotional disturbance may interfere with all aspects of intellectual activity and may be itself precipitated by these defects. The patient who becomes confused at a task tends to have a feeling of inadequacy which may lead not only to headache and outbursts of irritability but also to complete suppression for the time being of his powers of thinking: the phenomenon described by Goldstein as the catastrophic reaction.

(4) *Post-traumatic headaches.*—Anyone who is responsible for the rehabilitation of patients with head injury must formulate his ideas about the post-traumatic syndrome—the attacks of headache, dizziness, irritability and confusion which occur so commonly *after* the initial recovery from head injury. There are large gaps in our knowledge of this syndrome, and no little disagreement as to its nature. It is necessary, nevertheless, to have some working hypothesis, otherwise what shall one say to the man who complains of headaches during convalescence? I believe that almost every patient who makes a full recovery from concussion suffers at a certain stage of his recovery from headaches. In the mild head injuries the headaches may occur sporadically for some weeks and then disappear. In the severe cases the headaches may not come on until long after the patient has left hospital, and may not come on at all if there is any serious degree of residual organic defect. The patient must have recovered a certain amount of mental clarity before he appreciates headaches.

Now it is one thing to have a headache; it is another thing to complain about it. Although attacks of headache occur fairly constantly the reaction of the patient to them varies considerably, depending on a variety of factors, such as the emotional make-up of the patient, his anxieties and fears, his ability and desire to cope with his work once more. Emotionally stable, well-adjusted, and reliable witnesses—for example, most doctors—will describe their difficulties in concentrating when first they return to work; they will ascribe their headaches to attempts to concentrate, their headaches or dizziness to exertion or change of posture. Identical symptoms are complained of by other patients who are unstable and badly-adjusted, but nevertheless reliable witnesses. The difference is that the first type will manage to carry on with their rehabilitation with the minimum of interruption, while the second type are likely to break down on return to work unless they are given special treatment, treatment that inevitably comes within the purview of rehabilitation.

If this view as to the incidence of post-traumatic symptoms is correct then we must regard the syndrome as organic, just as syncope is; but, like syncope, it is influenced by emotional and psychoneurotic factors.

The early stages of recovery.—Rehabilitation begins when the patient begins to talk and respond properly. How does he discover that he has had a head injury? As his con-

fusion clears he slowly puzzles it out for himself, with the aid of explanations which come better from the doctor, with reassurance, than from the relations. The explanations and reassurance may need to be repeated more than once, for although the patient may be able to conduct a conversation in a manner that gives a superficial appearance of normality, yet he is at this stage confused, disorientated, and forgetful, for a period varying between minutes and weeks, according as the brain injury is mild or severe.

This is the stage at which assessment of the brain damage and of the type of the patient can first be undertaken. Without such investigations the rehabilitation cannot be adequately planned.

Getting up.—Notwithstanding the recommendations of Symonds these patients are often kept in bed too long, on the assumption that the liability to post-traumatic headaches is thus diminished. There is no evidence in favour of this view, and the practice becomes a bad one when, as so often happens, the next stage of rehabilitation is hurried.

There is rarely reason why the patient should not be allowed to get up a few days after he has recovered consciousness. Thus, a man whose total amnesia is six hours or less can be got up gradually towards the end of a week. If he gets a headache, he can be put to bed with some aspirin, and can get up again next day. Recourse to bed is, however, rarely necessary, for headache is not a conspicuous feature of this stage of recovery. The fact that the patient is got up early does not mean that he is to go back to work early. In cases of prolonged confusion and irritability, after unconsciousness of a week or more, the effect of sitting the patient out of bed and of giving him baths is often most soothing.

Graduated physical activities.—From the stage of getting up graduated physical (and mental) exercise may begin. It is necessary to grade the exercises, and the speed with which the patient passes from one stage to the next depends, not only on his progress with the exercises, but also on the estimated severity of his injury. For the mildly concussed the physical exercise can take first the form of walking and light physical training, thence by stages to more strenuous physical training, games, and heavy physical work. For the severely injured who, when they first get up, are still confused and even disorientated, light exercises to music, gentle indoor ball games, and deep breathing exercises are useful. These patients need much individual attention, and plenty of rest between exercises. Patience is necessary, also, for they often forget a game and need to have it explained to them all over again. No exercise should be pushed to the point of provoking a catastrophic reaction.

What is the value of physical exercise? It hardens the patient physically, thus preparing him to adjust himself the more easily to the physical demands of his normal life. It provides also a sense of achievement which is valuable in a man who is mildly confused and incapable of concentrated mental effort. It helps him to escape boredom. And it is perhaps also beneficial in modifying intracranial pressure.

At what stage should the patient be called upon to do violent physical training, Swedish exercises, and the like? Opinions differ on this question. There are some who would start it within a few weeks of quite severe injuries; others would introduce it more gradually and at a later stage. Before doing severe exercises the patient should, in my opinion, pass successfully through a stage of light competitive games.

Occupational treatment.—While physical re-education is going on handicraft can provide simple tasks within the powers of most patients, tasks which occupy their time at a stage when they are incapable of reading or talking consecutively for any length of time and which give them a sense of achievement: leather-work, basket-work, poker-work, weaving at a hand-loom, and book-binding. Heavier crafts such as carpentry, metalwork, weaving on large looms, and outdoor occupations, such as gardening and house-decorating, come later.

In craft work the teacher must constantly bear in mind that what really matters is not the initial standard of performance, but the degree of improvement shown from day to day. So often the star pupil of the class proves to be a psychoneurotic with headache after a trivial head injury.

Mental exercise.—The simplest mental exercises are those connected with movement, where the alternations of movement require concentration. For the confused patient simple games of a childish kind without competition are useful, for example, sorting cards according to colours, shapes, or what is written on them. It is an index of their degree of confusion that grown men will play these games with considerable pleasure.

In the later stages mental exercises should be directed towards the specific defect. Testing of the mental processes comes first and is in itself treatment. Special exercises can be introduced for lower level defects, such as those of reading and calculating. Sometimes it is possible to supplement the damaged functions, as, for example, by encouraging the patient with a defect of reading to trace or copy the words he is trying to read, or by teaching lip-reading to a patient whose difficulty is in understanding the spoken word. The prognosis depends on the residual learning capacity.

It is doubtful whether special, graded mental exercises can seriously compete with the patient's own attempts to re-educate himself, once he has, by testing, been shown the way; but the value of encouragement by means of continued supervision cannot be overestimated.

Visual treatment.—No patient can relearn intellectual tasks unless his sight is good, and as many of these patients have visual symptoms, diplopia, phorias, or errors of refraction, it is important that ophthalmological treatment should be given whenever necessary.

Psychological factors.—The importance of psychological factors has already been indicated, and no attempts at rehabilitation are likely to be successful unless the patient's anxieties and fear are assuaged and unless he is helped through the phases of depression and the other disturbances of feeling that so often beset him during recovery from head injury.

The final test.—It is very difficult in hospital or convalescent institution to provide a test of full recovery, and the final test is the patient's return to work. It is the duty of those in charge of rehabilitation to see that the man is adequately supervised during this period, and that any special points concerning graduation of his work in the initial stages should be made known to his family doctor, his works doctor, or his Unit medical officer.

Dr. W. Russell Brain: For a long time it has seemed to me that the high incidence of neurosis after injury, particularly after industrial injuries, and our continued neglect to deal with it as a substantial medical and social problem is a considerable reproach to us as doctors. The first step must necessarily be an attempt to ascertain why traumatic neurosis occurs. This question can be approached in two ways, either by a psychological investigation of patients suffering from neurosis after injury, or by a statistical inquiry into the characteristics shown by a group of such patients. The two methods are supplementary. Psychological investigation of injured individuals is difficult for many reasons. My method this afternoon is the second one and I shall concern myself only with such psychological facts as seem to emerge from a study of the group as a whole.

I have long had an impression that traumatic neurosis occurs much more frequently in patients suffering from the effects of industrial injuries than in those injured in road accidents, and this supposed difference suggested itself as a promising basis for an inquiry. I have therefore taken as my material 100 consecutive cases of male patients suffering from the effects of a head injury acquired in a road accident, and 100 consecutive cases of male patients suffering from the effects of an industrial head injury. All patients were seen some time after their injury, the average interval before they came under observation being ten months. I have divided the patients in each group into three subgroups according to whether their head injuries were mild, moderate or severe. I have called mild those injuries in which either consciousness was not lost or the patient was merely dazed for a short time. I have called moderate those injuries in which consciousness was lost, but the patient had recovered normal mentality in twenty-four hours and I have classified as severe all cases in which loss of consciousnes or mental confusion lasted for more than twenty-four hours. The state of consciousness, however, though important, is not the sole criterion of the severity of a head injury and I have taken into account severe focal cerebral contusion when this occurred with only brief loss of consciousness. I have also divided each group into three sub-groups according to whether I consider the patient's symptoms to be purely organic, purely neurotic or mixed. It is clear that this classification depends to a considerable extent upon personal judgment. There is no difficulty in deciding about most hysterical symptoms. In assessing the nature of other symptoms I have depended upon such criteria as the characteristics of the headache, especially its constancy or otherwise and its relationship to precipitating factors, the effect of the passage of time upon symptoms and the attitude of the patient to them. No doubt others would have classified individual cases differently, but perhaps this is not of great importance since the same methods have been applied to all the cases by the same observer.

INCIDENCE OF NEUROSIS AFTER ROAD ACCIDENTS AND INDUSTRIAL INJURIES

Table I shows the frequency with which neurosis follows head injuries (1) after road accidents and (2) after industrial accidents.

TABLE I.

	Neurotic	Mixed	Organic
Road accidents—100 cases ...	8	15	
	23		77
Industrial accidents—100 cases ...	23	32	
	55		45

The next step is to inquire whether there is any correlation between the incidence of neurosis and the severity of the injury. This is shown in Table II.

TABLE II.

		Neurotic	Mixed	Organic	Total
Road accidents—Severe	...	1	11	48	60
Moderate	...	3	2	18	23
Slight	...	4	2	11	17
Total		8	15		
		23		77	100
Industrial accidents—Severe	...	4	8	22	34
Moderate	...	8	12	10	30
Slight	...	11	12	13	36
Total		23	32		
		55		45	100

Table II shows, first, that the injury is severe in a much higher proportion of patients who have had road accidents 60% compared with 34% of those who have had industrial accidents; and secondly that the industrial group shows a high incidence of neurosis associated with the less severe injuries, which is not present in the road accident group. This is better shown in Table III.

TABLE III.

	Neurotic and Mixed	Total	Percentage
Road accidents—Severe	12	60	20
Moderate and slight ...	11	40	27
Industrial accidents—			
Severe	12	34	35
Moderate and slight ...	43	66	65

It is quite clear that a severe head injury as such is not an important cause of traumatic neurosis, but we have still to explain the apparently paradoxical correlation between neurosis and the slighter injuries.

It must be remembered that we are here dealing not with totals of injured persons, but with persons selected from the total number injured because the severity of their symptoms (1) in the road accident group calls for compensation (2) in the industrial accident group incapacitates them for work. It will generally be agreed that the incidence of severe head injuries is much higher in those who have been involved in road accidents than in a group exposed to the varied hazards of a large number of industries. Allowing for the fact that in some industries the risk of head injuries is much greater than in others it is still true that a mixed group of industrial workers is exposed to somewhat rare severe injuries, and fairly frequent moderate or slight injuries. If now the incidence of neurosis is independent of the severity of the injury, if, in other words, there exists

in the exposed community a proportion of individuals who react to even a slight injury by developing a neurosis, the high proportion of less severe injuries will lead to a selection of these susceptible persons, since those with slight organic symptoms will soon return to work and therefore will never reach the neurologist. Hence there will be an apparently high incidence of neurosis complicating the slighter injuries, in the industrial group.

But in the industrial group the 35% incidence of neurosis complicating severe injuries is significantly higher than the 20% in the road accident group which may perhaps be regarded as a sample of the general population at these ages; and the generally raised liability to neurosis in the group calls for explanation.

AGE AND OCCUPATION

There is no significant difference in the average age of patients in the two groups, nor between the average ages of those with and those without neurosis in either group, so that there is no evidence that age plays any part in the ætiology of traumatic neurosis.

There are significant differences in the incidence of neurosis in different occupations in both groups. This is shown in Table IV.

TABLE IV.

	Occupation	Total	Neurotic	Percentage
Road accidents	Professional and clerical ...	38	4	11
	Skilled artisans	27	5	19
	Light unskilled	14	6	43
	Heavy unskilled	19	7	37
	Unclassified	2	1	—
Industrial	Professional and clerical ...	2	—	—
	Skilled artisans	20	7	35
	Slight unskilled	19	10	53
	Heavy unskilled	59	38	64

This table shows first that in both groups the incidence of neurosis is highest in the unskilled labourers; in fact out of 23 patients in the industrial group who developed neurosis after slight injuries 17 were heavy unskilled labourers. Secondly, men of any occupation are substantially more likely to develop traumatic neurosis if they are injured in an industrial accident, even though their organic injury is likely to be less severe. I would briefly suggest two reasons why a slighter industrial injury is more likely to produce neurosis than a more severe road accident.

First, an industrial injury is an occupational injury, as a road injury usually is not. It therefore suggests to the workman that his occupation is a dangerous one, and it is likely to cause a sense both of physical danger and of economic insecurity. Second the legal procedure is widely different in the two groups. In a road accident the insurance system is a guarantee of compensation in most cases: in the machinery of the Workmen's Compensation Acts it operates in the opposite sense, since the workman's right to compensation is repeatedly under review and frequently contested. Hence although the workman injured at work receives immediate compensation which his fellow knocked down by a car does not, his economic security is really far more seriously threatened. There are other defects, of a similar kind, in the Workmen's Compensation Acts which contribute to the development of neurosis but which I cannot now discuss.

SUGGESTED REMEDIES

(1) Rehabilitation in all cases of slight injury begins with the general practitioner or casualty officer who first sees the patient. These front-line workers need to learn the right psychological handling of the injured man; to avoid suggesting serious injury when none exists and equally "a narrow escape". They should learn also to avoid the hospitalization of really slight cases.

(2) All big centres need units of doctors trained to deal with head injuries, both slight and severe. In this way only is it possible to avoid the ill-effects of scattering these patients in general wards under the care of surgeons who have neither the knowledge nor the interest needful.

(3) Occupational therapy should merge into therapeutic occupation, i.e. organized light work, adjusted to each man's capacity.

(4) The social responsibility for the injured should be more widely recognized and the emphasis changed from compensation to rehabilitation. The need for compensation is to a large extent a measure of the failure of rehabilitation.

(5) The Workmen's Compensation Acts should be revised so that an industrial injury should not immediately involve a potential dispute about the ownership of a sum of money. Medical issues should be decided by medical boards closely linked with rehabilitation units; and an adequate maintenance allowance should be guaranteed to the injured man as long as the medical board regarded him as disabled and as long as he co-operated in his treatment and rehabilitation.

(6) At the same time it is important to avoid an exaggerated paternalism. Here we have to face an aspect of the largely unsolved problem of modern society, how to provide social services without robbing the individual citizen of his sense of responsibility for his own welfare. There would be no traumatic neurosis if all the injured were like an Irish hunting woman who consulted me because after the last of many falls she thought her double vision was worse than it used to be. Such toughness is doubtless partly innate, partly cultural. Society can do a good deal to foster it if it is conscious of the need. As doctors we have the double task of educating both individuals and society.

Dr. Ludwig Guttmann: Rehabilitation after peripheral nerve lesions means restoration of the working capacity of the injured person. It includes, apart from the actual surgical treatment, all methods which accelerate functional recovery:

(1) Therapeutic arrangements of a more passive or preventive nature, such as precautions for keeping the paralysed limb in the right position with and without splintage and physiotherapy.

(2) All arrangements which accelerate functional recovery with the patient's active co-operation until he is enabled to resume his former occupation, or failing that to do useful alternative work in the same industry. Arrangements of this group are (*a*) remedial exercise; (*b*) occupational therapy; (*c*) some physiotherapy; (*d*) reconditioning.

(3) Vocational training, i.e. training of those crippled by peripheral nerve injuries for special occupations adapted to their permanent disability.

As there are some transitions between the individual groups this distinction may not be considered as absolutely strict. According to this definition it is obvious that rehabilitation after peripheral nerve lesions has to start immediately following injury. Dr. E. A. Nicoll's opinion expressed on this subject in a recent paper on fractures "Rehabilitation starts on the first day of treatment" can be accepted in the full meaning of the words also for peripheral nerve lesions.

General organization.—The installation in this country of several centres for the treatment of peripheral nerve injuries is a great step forward. The congregation of cases in a single department under the same specialized staff, with continuous treatment under the same supervision, is certainly the best guarantee for a systematic study of the whole question, and for better results. The success of a centralized treatment and care of peripheral nerve injuries in other countries was shown by the "Peripheral Nerve Centres" in the U.S.A. during the last war and particularly by Foerster's work in Germany during and after the last war. His material included about 4,000 cases. Although he worked under conditions by no means ideal compared with those of a modern centre in this country, his results were remarkably good and better than those of many other authors of that time. Foerster has emphasized again and again the secret of his better results. It was only in some respects a specialized surgical technique; the main reason was a better and systematic after-treatment and after-care, in other words, a good understanding of rehabilitation.

The installation of centres for peripheral nerve injuries, however, does not cover the whole problem of organization in the rehabilitation work. In practice it is not possible to bring all cases into these centres, particularly in the early days after injury. Therefore precautions should be taken in all General and Military hospitals, *particularly in Military Base-Hospitals*, that the injured can be seen immediately by a Nerve Specialist versed in the after-treatment of peripheral nerve lesions. Neglect of this vital principle of rehabilitation in the first period, even in the first days after injury, accounts for much of the prolonged disability of the injured person, with all its economic consequences. The

importance of this point can hardly be exaggerated. An integral part of the organization of what might be called "Primary rehabilitation service" is a thorough record of all treatment given in the first period after nerve injury. Undoubtedly such a service would greatly facilitate the work of the centres for peripheral nerve injuries and would play a big part in improving the end-results.

Of the same importance as the primary supervision immediately after injury is the late supervision of these cases after their discharge from hospital, from the centres and from the Army. This late supervision also includes the post-war supervision of peripheral nerve injuries. Experiences in all countries after the last war have clearly shown that any successful late supervision of these cases can only be achieved by a loyal co-operation of the medical authorities with the public health services and—as Cairns and Young pointed out (1940)—with the Ministry of Pensions and, last but not least, with the employers. Such an organized co-operation of the various authorities concerned with the rehabilitation work is of particular importance in the reconditioning period of the injured. One of the main tasks of the "after-care service" is (1) to provide the injured man with light and graduated work in his former occupation until he is fit for heavy work; (2) to supervise this light and graduated work. In my own experience the best results in supervising the injured persons during the reconditioning period were obtained with the help of industrial medical officers and general practitioners. Experiences in all countries have shown that many patients, left alone in the reconditioning period, will never make sufficient effort to reach their full working capacity.

In discussing some methods of particular importance for a speedy and, if possible, complete rehabilitation only a few points can be considered. Cases with peripheral nerve lesions can be grouped into those in which restoration of nerve conduction is possible and those in which there is no chance of nerve regeneration. In regard to treatment, however, this distinction is not an absolutely strict one as similar principles have to be considered in both cases up to a certain point.

POSITION OF PARALYSED LIMBS

The position of paralysed limbs follows the principle of close approximation of the points of attachment of the paralysed muscles. The principle underlying treatment is to maintain and increase elasticity of the affected muscles. All experts on the subject agree that overstretching of a paralysed muscle even in the very first period after injury means a severe and often irreparable additional damage of the paralysed muscle. In 1916 Sir Robert Jones expressed it very clearly: "The most skilful operation performed on the most suitable case will prove a fiasco unless the affected muscles are continually kept relaxed until recovery takes place." Unfortunately, this well-known and most essential point is in practice not always duly considered and may even be completely neglected. It is for instance amazing how often this principle is neglected in cases of ulnar and median nerve palsy in spite of the fact that special splints have been described for the approximation of the intrinsic muscles of the hand.

In preventing the claw position of the fingers in cases of ulnar nerve palsy two types of splints are recommended. The one is designed to maintain the proximal phalanges in a position of medium flexion, at the same time preventing flexion of the middle and terminal phalanges. The other, recommended particularly for isolated paralysis of the interossei, maintains the greatest possible extension of the long flexors of the fingers by means of narrow elastic splints which are applied to the dorsal side of the fingers, thus extending all phalanges as far as possible. The advantage of these splints, according to Foerster, lies in the fact that the middle and terminal phalanges remain sufficiently stretched during all the finer activities of the fingers in which small objects are grasped and moved between the tips of thumb and index or middle finger.

In median nerve palsy, in which relaxation of the thenar muscles is so important, splints have also been designed to bring the thumb into a position of abduction and opposition while its terminal phalanx is extended. Among other authors Foerster (1929) has recommended such a splint, which, however, tends to be too inflexible. On the other hand splints, such as recommended by Sumner L. Koch and Michael L. Mason (1939), which are more flexible have the disadvantage that the thumb is held in adduction and in too strong flexion at its metacarpo-phalangeal joint, and they do not give the necessary abduction and opposition of the thumb. The problem of suitable splints for isolated median palsy and also for combined median and ulnar or radial palsies is therefore still

unsolved. Whatever splintage may be used it is of vital importance that any direct pressure of the splint on the paralysed muscle must be avoided, and "splint-free" intervals should be given.

STRENGTHENING OF SYNERGISTS

The taking over of the function of a paralysed muscle by one or several of its normal synergists can be of great practical value in rehabilitation. Besides the well-known compensatory function of the brachioradialis in a biceps palsy and other instances the following example illustrates this principle: In a case of complete paralysis of the axillary nerve abduction of the arm may be carried out astonishingly well by the supraspinatus muscle. It is possible in such cases to dispense with splints altogether and to restore function and working capacity by strengthening such synergistic muscles.

ELECTROTHERAPY

It is one hundred years since John Reid in Edinburgh (1841) first described the beneficial effect of galvanic current on denervated muscles. Since then opinions about the value of electrotherapy in the treatment of peripheral nerve lesions have oscillated a great deal. Experiments on the subject do not allow satisfactory conclusions, and even the great clinical experience of the last war has not settled this problem. Yet experts are agreed that electrotherapy is useful in accelerating rehabilitation after peripheral nerve lesions. My own experience has endorsed the value of electrotherapy carried out by galvanic exercise of the paralysed muscles. If carried out regularly and properly by a reliable person having the necessary knowledge of the anatomy and physiology of movement and under permanent medical supervision it is a valuable auxiliary method in the treatment of atrophy and in maintaining or improving the elasticity of paralysed muscles. This has been proved recently by an experimental study on galvanic treatment of denervated muscles in rabbits carried out in Dr. J. Z. Young's Department of Comparative Anatomy in the University of Oxford by Dr. Ernest Gutmann and myself (1942). Although in these experiments the daily galvanic exercise of the paralysed muscles did not entirely prevent the onset and progress of atrophy immediately after denervation, it had, however, a definite delaying and diminishing effect on the atrophy in later stages. Moreover it accelerated the recovery from atrophy, once the muscles had become reinnervated and recovery of function had commenced. The histological findings in our cases eliminate the suspicion that the greater volume of the treated muscles might be the effect of a hypertrophy of the connective tissue. Exactly the reverse was found, for the treated muscles showed far less fibrosis.

It may be noted that in cases of complete paralysis galvanotherapy is the only method (in contrast to massage) which enables the paralysed muscles to exercise their original function—or to put it in Foerster's own words: "Electrotherapy reminds the paralysed muscle of its normal task." Furthermore electrotherapy is most useful in augmenting active exercise in those cases in which regeneration is taking place but the patient cooperates poorly. On the other hand, it would be overrating the value of the method to imagine that atrophy of muscles can be prevented or considerably diminished in all cases of denervated muscles. In my own cases in which great vascular damage had occurred in addition to the nerve injury or in which the muscles themselves had been very considerably damaged the beneficial effect of galvanic treatment was not so convincing.

REMEDIAL EXERCISE

Active exercise is of *cardinal* importance in achieving the most complete and quickest rehabilitation. In recovering lesions three different stages require special consideration:

(1) As long as voluntary movements are still weak the exercises should only be directed towards overcoming the inertia of movement, and should not work against gravity. The simplest way to achieve this is by placing the limb in such a position that movements are carried out in the horizontal plane. Exercises in a bath are in some cases helpful.

(2) Having overcome the inertia of the limb without any other help, exercise should be attempted against gravity.

(3) If the muscle is able to move the limb against gravity, graduated weights are added against which the muscle has to work.

The principle of the exercises is to effect quick movements over the widest possible range. The movements are followed by fairly long rests, after which they are again repeated. This kind of exercise has always to be supervised since the patient when left alone is usually inclined to exhaust himself in multiple partial performances as opposed to a few maximal responses which are of greater benefit. Since many patients never make progress without assistance a *daily* supervision of active exercise by the doctor has undoubtedly the best effect in obtaining the patient's energetic co-operation and unremitting effort which are so necessary for successful rehabilitation.

OCCUPATIONAL THERAPY

Occupational therapy at the centres for peripheral nerve injuries might be a valuable addition to active exercise treatment. In cases where restoration of nerve conduction is possible it will accelerate rehabilitation. In cases of permanent paralysis it will help to develop and to improve subsidiary and trick movements. It should, however, be emphasized that in order to build up occupational therapy as a really useful and reliable method for accelerating rehabilitation, a carefully elaborated organization and a plan of indication, time of onset and duration, have to be established. These, as far as I know, have not yet been developed in regard to peripheral nerve lesions. Although N. A. Haworth and E. M. Macdonald (1940) published a very suitable list of suggested occupations in peripheral nerve lesions and some authors let their patients work with suitably altered tools, a special technique of occupational training is not yet fully formulated, and the various crafts used in occupational training have not yet been analysed and suitably modified from the physiological and psychological point of view. In a median or ulnar nerve paralysis, for instance, all the arrangements for occupational training must be conditioned by the anæsthetic and atrophic state of the skin and subcutaneous tissues. Exercises which can macerate the skin such as with moist clay, must be avoided, also tools producing a permanent and too strong pressure. Therefore in every case clear direction should be given to the occupational therapist about the details of motor, sensory and trophic disturbances and supervision of this therapy by the doctor is of great importance. A close co-operation between doctor and occupational therapist is also of immense value for the mental state of the patients, particularly in overcoming the various mental disabilities due to injury and hospitalization. The latter particularly, should not be underestimated in war time. In every case the occupational therapist should record all his arrangements and observations, for these can be of great help to the doctor, giving information about the patient's behaviour with regard to the restoration of working capacity.

LITERATURE

CAIRNS, H., and YOUNG, J. Z. (1940), *Lancet* (ii), 123.

FOERSTER, O. (1929), "Handbuch der Neurologie". Berlin, Part II, Sections 2 and 3.

FRAZIER, C. H. (1920), *Ann. Surg.*, **7**, 1.

GUTMANN, E., and GUTTMANN, L. (1942), *Lancet* (i), 169.

HAWORTH, N. A., and MACDONALD, E. M. (1940), "Theory of Occupational Therapy". London.

JONES, ROBERT (1916), *Brit. M. J.* (i), 641.

Id. (1928), *ibid.* (ii), 639.

KOCH, S. L., and MASON, M. L. (1939), *Surg. Gynec. & Obstet.*, **68**, 1.

REID, J. (1841), *J. Med. Sci.*, **1**, 320.

JOINT DISCUSSION No. 2

Section of Therapeutics & Pharmacology with Section of Medicine

Chairman—R. D. LAWRENCE, M.D., F.R.C.P.
(President of the Section of Therapeutics and Pharmacology)

[*November* 11, 1941]

DISCUSSION ON THE KIDNEY AND HYPERTENSION

Professor Arthur Ellis: The problem of hypertension and the kidney has interested clinicians since the time of Bright. When the occurrence of hypertension was first appreciated its dependence on disease of the kidney was generally assumed. Doubt as to the invariability of this association was first aroused by the remarkable observations of Mahomed (1874) of Guy's Hospital, who described patients with hypertension without albumin in the urine. There followed the clinical observations of Allbutt (1895) and of Huchard (1899), who described cases of long-standing hypertension without clinical evidence of renal disease. There thus arose the conception of an essential or primary hypertension to be distinguished from the secondary hypertension due to chronic renal disease. Recently the experiments of Goldblatt *et al.* (1934) who produced sustained hypertension in dogs by means of screw clips on the renal arteries, have led some students of Bright's disease to return to the old belief that all hypertension is renal in origin. The proponents of this argument usually suggest renal arteriolosclerosis, with resulting diminished blood-flow through the kidney, as the responsible mechanism in essential hypertension. There are strong arguments against a too hasty acceptance of this thesis. It is, of course, quite possible that essential hypertension is due to some extrarenal factor—endocrine or other—which causes a functional diminution of blood-flow through the kidney, but the evidence at present available suggests that renal arteriolosclerosis is the result not the cause of the hypertension. For we see: (1) that broadly speaking the longer the duration of the hypertension the greater the degree of renal arteriolosclerosis (Turnbull, 1915); (2) that in malignant hypertension the arteriolar lesions in the kidney are minimal in the early stages and severe in the later stages (Ellis, 1938); (3) that if hypertension is produced in a rat by clamping one renal artery, arteriolar lesions will appear in the unclamped kidney due to the hypertension but will be absent in the clamped kidney which is protected from the hypertension by the clamp on its renal artery (Wilson and Byrom, 1939).

We must conclude that the evidence that essential hypertension is due to renal vascular lesions is still insufficient. Until further evidence is available it seems to me desirable to retain the conception, which we owe to Allbutt, of essential hypertension in contrast to the hypertension secondary to renal disease.

This separation of essential hypertension from the hypertension of chronic nephritis was an important advance in our knowledge of "the kidney and hypertension", but it did not satisfactorily solve the problem because, as many observers began to note, certain cases which appeared to be examples of primary hypertension died in uræmia and showed at post-mortem the histological changes of chronic nephritis. These are the cases which are now generally recognized as malignant hypertension (Volhard and Fahr, 1914; Keith, Wagener and Kernohan, 1928; and Fishberg, 1931). The recognition of malignant hypertension was of primary importance in the solution of our problem, but its significance was for long—and generally indeed is still—not appreciated.

In a previous communication (Ellis, 1938) I pointed out that in the stage of malignant hypertension when symptoms first appear clinical evidence of renal impairment is often lacking or minimal, and that histological examination of the kidneys of patients dying in this stage shows little or no evidence of nephritis, arteriolar necrosis being apparently the earliest histological change. We have now studied 103 examples of malignant hypertension. Albumin was absent from the urine of 10 when first seen. In 26 there was only slight albuminuria and the renal function tests were normal. We have examined the kidneys in 12 cases dying from a non-renal cause such as cerebral or subarachnoid hæmorrhage, cardiac infarction or failure. None of these kidneys showed extensive damage, the renal parenchyma was well preserved; in some the lesions were so scanty that only careful search revealed them. The earliest lesions appeared to be arteriolar necrosis. Fahr was the first to appreciate the significance of these arteriolar lesions, he considered them the cause of the glomerular lesions. He attributed them to various toxins —syphilis, lead, rheumatism and various other unknown agents. Volhard considered that both arteriolar and glomerular lesions were due to vascular spasm. We thought that the glomerular changes were due to the arteriolar lesions and that these were a direct result of the hypertension. The production by Wilson and Byrom, in designed experiments, of these arterial and glomerular lesions would seem definitely to establish their hypertensive origin. Furthermore, the histological picture in the rat with experimental hypertension closely resembles "chronic interstitial nephritis" in man. This conception that hypertension can produce changes in the kidney formerly regarded as chronic nephritis is essential to an understanding of chronic Bright's disease.

A major difficulty in the understanding of Bright's disease is that different renal disorders may, in their late stages, show a very similar clinical picture consisting of hypertension, renal failure, and hypertensive retinitis with papillœdema. Histologically the same difficulty occurs, the kidneys showing a similarity of histological change which has made their differentiation difficult. This end-stage is often designated "chronic interstitial nephritis". Most close observers of Bright's disease have long recognized that "chronic interstitial nephritis" is not an entity but includes a number of different conditions: chronic nephritis, malignant hypertension, chronic pyelonephritis, the late stage of a toxæmia of pregnancy which has not cleared up, the "chronic interstitial nephritis" of lead workers, even the amyloid kidney may terminate with the clinical and histological picture of "chronic interstitial nephritis" superimposed on amyloid disease. All these conditions are associated, when this syndrome develops, with hypertension. We believe that the syndrome and its associated histological picture are the result of this hypertension. This is the explanation for the similar end-stage of such otherwise varying conditions. We envisage the common factor to be renal ischæmia. The progressive course of the condition we attribute to the vicious circle demonstrated by Wilson and Byrom (1941) in rats—renal ischæmia leads to hypertension which in turn gives rise to destructive vascular lesions, these lead to further renal ischæmia and so augmented hypertension—a progressive process.

When the occurrence of these common hypertensive lesions is appreciated the histological differentiation of the underlying conditions is simplified and with the assistance of the clinical history a separation of the various conditions is usually possible. The term chronic interstitial nephritis should therefore be dropped. Chronic hypertensive Bright's disease is composed of a number of entities including chronic nephritis, benign and malignant hypertension, chronic pyelonephritis, the hypertension following toxæmia of pregnancy and various other odd conditions. The separation of these various entities is most easily achieved by careful observation of the natural history of their development. Since hypertension is common to them all it is not surprising that the

morbid anatomist viewing the end-stage has found difficulties of interpretation, or that the pathological classification of Bright's disease has been traditionally confused.

REFERENCES

ALLBUTT, C. (1895), *Tr. Hunter. Soc.*, 1895-96, p. 38.
ELLIS, A. (1938), *Lancet* (i), 977.
FISHBERG, A. M. (1931), "Hypertension and Nephritis". Philadelphia.
GOLDBLATT, H., LYNCH, J., HANZAL, R. F., and SUMMERVILLE, W. W. (1934), *J. Exper. Med.*, **59**, 344.
HUCHARD, H. (1899), "Traité clinique des maladies du cœur". Paris.
KEITH, N. M., WAGENER, H. P., and KERNOHAN, J. W. (1928), *Arch. Int. Med.*, **41**, 141.
MAHOMED, F. A. (1874), *Brit. M. J.* (i), 585.
TURNBULL, H. M. (1915), *Quart. J. Med.*, **8**, 201.
VOLHARD, F., and FAHR, T. (1914), "Die Brightsche Nierenkrankheit". Berlin.
WILSON, C., and BYROM, F. B. (1939), *Lancet* (i), 136.
Id. (1941), *Quart. J. Med.* (New Series), **10**, 65.

Dr. Clifford Wilson: *Histological Evidence on the Relation of Hypertension to Renal Disease.*—In the progress of patients with Bright's disease two of the most striking features seem to be: (1) The similarity of the terminal stages in different types of Bright's disease, a similarity which is often reflected in the histological changes in the kidney; (2) the rapid deterioration which often takes place when the blood-pressure rises to levels of 200 mm.Hg or more. Professor Ellis has outlined the conception of a vicious circle which it appears may help to explain these features, the essential aspects of the vicious circle being the production of hypertension following renal ischæmia on the one hand, and the production of obstructive renal arterial lesions by hypertension on the other.

Volhard and Fahr (1914) established the existence of a form of essential hypertension in which death occurs from uræmia. Histologically the condition is characterized by severe acute vascular lesions in the kidney, so-called acute fibrinoid necrosis of the arterioles, and endarteritis of the smaller arteries. Volhard and Fahr termed this condition "malignant nephrosclerosis" and subsequently it became more generally known as malignant hypertension. The clear separation of this malignant form of essential hypertension is the great contribution of Volhard and Fahr to our knowledge of Bright's disease. The importance of maintaining this separation has not been appreciated and in recent years, particularly in America, the term "malignant hypertension" has been applied to cases of chronic nephritis and chronic pyelonephritis with a severe terminal high blood-pressure and clinical features, such as papillœdema, resembling those of malignant hypertension. Thus the distinction made by Volhard and Fahr is in danger of being confused and the true identity of malignant hypertension again obscured. The term "malignant hypertension" should be confined to the malignant type of essential hypertension, thereby maintaining the contrast with the more common benign (essential) hypertension. The terminal hypertensive phenomena in other forms of Bright's disease can if desired be described as a "malignant termination".

It is perhaps desirable first to describe the arterial lesions of malignant hypertension described by Fahr, i.e. fibrinoid necrosis and endarteritis. These occur in the kidney and other organs:—pancreas, intestine, suprarenal, retina, testis, in that order of frequency.

Fig. 1 shows typical examples of acute fibrinoid necrosis of an afferent arteriole to a glomerulus, and of endarteritis, or cellular intimal thickening, of an interlobular artery. It seems probable that endarteritis results from organization of fibrinoid necrosis in the smaller arteries.

Professor Ellis has presented evidence for the view that in malignant hypertension, renal damage is secondary to the hypertension, being minimal in the early stages and increasing as the disease progresses. Figs. 2, 3 and 4 are low-power views of the kidney from cases of malignant hypertension at different stages. Fig. 2 shows almost complete absence of histological change in the kidney; fig. 3 shows a moderate renal involvement, and fig. 4 a severe degree of renal damage, with focal interstitial fibrosis and tubular dilatation. It is this picture which has led to the confusion between malignant hypertension and chronic nephritis and resulted in the inclusion of both conditions under the heading "chronic interstitial nephritis".

The arterial lesions illustrated in fig. 1 are constantly found in malignant hypertension. They are also found, with the same organ distribution, in other types of Bright's disease

when severe hypertension has been present. This has not only led to difficulty in the histological diagnosis of malignant hypertension but has been the main obstacle to the recognition of this condition as a separate disease by the pathologist. From fig. 2 it will be obvious that in the early stages there is no danger of confusing the histological picture with that of chronic nephritis; on the other hand it may be difficult, and very occasionally it is impossible, to distinguish between the kidney in the advanced stages of malignant hypertension (fig. 4) and in a long-standing case of chronic nephritis in which endarteritis and fibrinoid necrosis of arterioles are present. (By "long-standing" chronic nephritis I mean those cases in which the disease has been present for many years or even decades, and in which the kidney shows the typical focal fibrosis.) The histological differentiation between malignant hypertension in the late stages and long-standing chronic nephritis is based on the following considerations: (1) Renal contraction is usually much more marked in chronic nephritis; (2) the glomeruli are greatly reduced in number in chronic nephritis but only slightly reduced in malignant hypertension; (3) a large number of glomeruli, often the majority, appear normal in malignant hypertension—relatively few in chronic nephritis; (4) the abnormal glomeruli show a greater variety in size and in type of lesion in chronic nephritis; the "type lesion" being a relatively large glomerulus showing increased cellularity, loss of lobulation and more or less extensive capsular adhesions. In malignant hypertension acute glomerular necroses are more common, and form the predominant lesion.

These histological differences between malignant hypertension and chronic nephritis are explained by the different natural history of the two diseases. In malignant hypertension we have a severe initial hypertension, acute vascular lesions dominate the picture, and the course is rapid so that death usually occurs before renal destruction is far advanced. In chronic nephritis severe hypertension is usually a late feature, whilst the renal damage has progressed slowly over many years and the resulting renal contraction is usually severe.

Having discussed the differences between malignant hypertension and chronic nephritis, let us again consider the vicious circle which plays such an important part in both diseases. The evidence which I shall present is derived from the study of experimental hypertension in animals.

Wilson and Pickering (1938) and Goldblatt (1938) noticed that when hypertension was produced in rabbits and dogs respectively, by clamping both renal arteries, these animals often developed hæmorrhages in the gut. Histologically, arterial lesions were found closely resembling those of malignant hypertension. These arterial lesions were not found in the kidneys, whence it was inferred that they were caused by hypertension, from which the kidneys were protected by the clamps on the renal arteries.

About this time, Byrom and I devised a method of determining the blood-pressure in the rat, which made it possible to follow the course of experimental hypertension in this animal (Byrom and Wilson, 1938). Following a technique similar to Pickering's, we were then able to produce hypertension by applying a silver clip to the renal artery and found that in the rat, in contrast to the rabbit and the dog, a permanent hypertension frequently resulted when *one* renal artery was partly occluded, the other kidney being left intact. It was thus possible to study the effect of experimental hypertension on an intact kidney.

(1) We discovered that when a sudden rise in blood-pressure to a high level, e.g. over 200 mm.Hg followed renal artery compression, acute vascular and glomerular lesions were produced in the *unclamped* kidney within a few days. No such lesions were present in the clamped kidney, which appeared in most cases histologically normal. These vascular and glomerular changes show a close resemblance to those of malignant hypertension in man (Wilson and Byrom, 1939).

It appeared, therefore, that lesions of the renal glomeruli and arterioles which had previously been thought characteristic of nephritis could be caused by hypertension. Since one kidney was intact at the onset, renal failure could not be a causative factor (confirmed by blood-urea determinations) and since the lesions were absent from the clamped kidney, a circulatory toxin or chemical agent appeared to be excluded.

(2) The next step was the finding in rats with sustained hypertension lasting many months, of chronic renal changes closely resembling chronic interstitial nephritis in man (Wilson and Byrom, 1941). These apparently represented the healed or healing stages of the acute lesions but the renal damage was more extensive, and acute and chronic lesions were often present together. These changes also were confined to the unclamped kidney, the clamped kidney appearing histologically normal. The lesions affected glom-

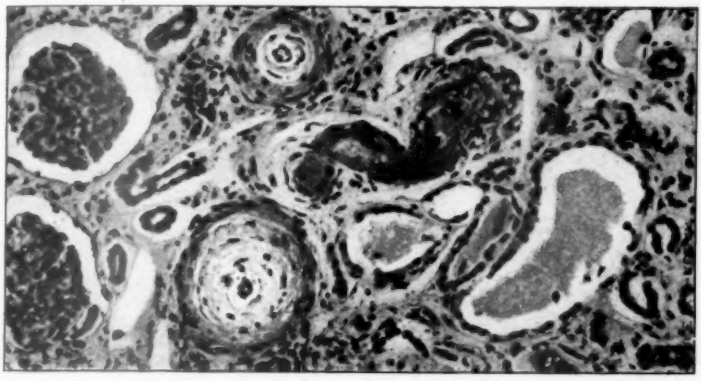


FIG. 1.—Kidney, malignant hypertension. Endarteritis of interlobular artery and fibrinoid necrosis of afferent arteriole. (Hæmatoxylin and eosin. × 150.)

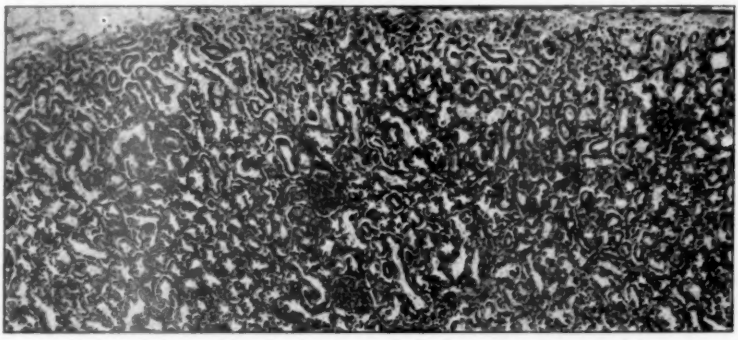


FIG. 2.—Kidney, malignant hypertension. Early stage showing apparently normal kidney. (Hæmatoxylin and eosin. × 44.)

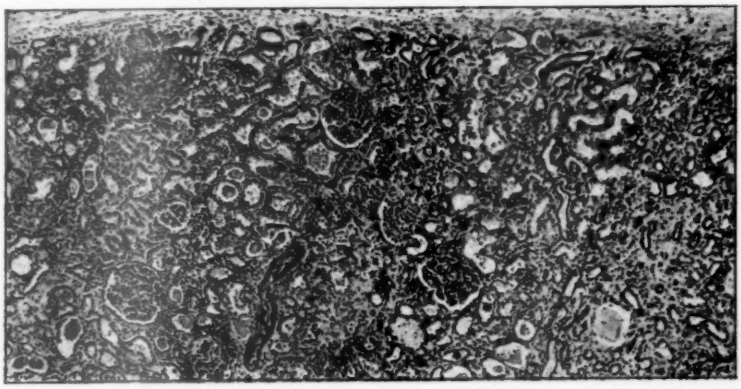


FIG. 3.—Kidney, malignant hypertension. Moderate renal damage. (Hæmatoxylin and eosin. × 44.)

eruli, tubules, interstitial tissue and arteries, and were focal in distribution, producing the familiar picture of focal fibrosis and tubular dilatation (fig. 5).

In view of the focal distribution and the close relation of the parenchymal changes to the arterial lesions it seems justifiable to conclude that this picture of chronic interstitial nephritis is a purely vascular process, resulting from high blood-pressure. Why all patients with hypertension fail to develop this picture in the kidney is not clear. Its production may be related to sudden development or to exacerbations of the hyper-

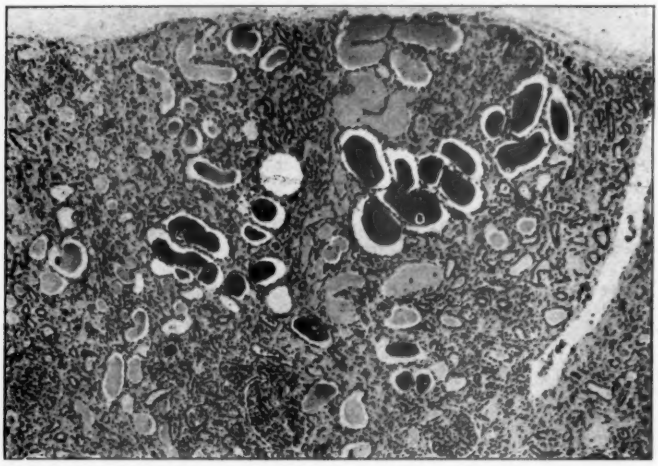


FIG. 4.—Kidney, malignant hypertension. Late stage showing focal fibrosis and tubular dilatation. (Hæmatoxylin and eosin. × 44.)

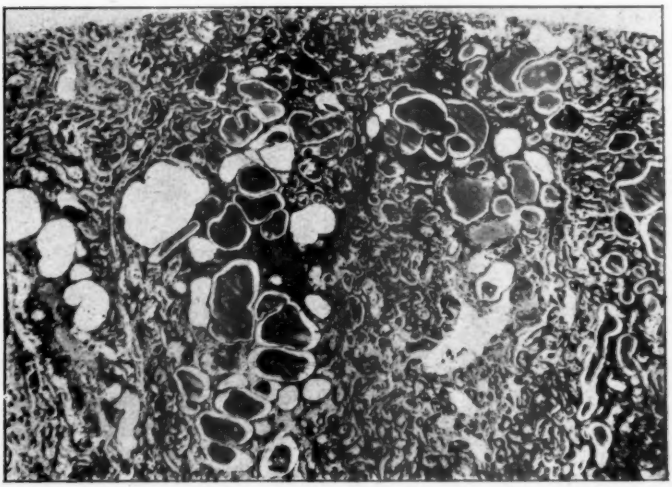


FIG. 5.—Unclamped kidney of rat with chronic hypertension. Showing similar extensive fibrosis and focal tubular dilatation. (Hæmatoxylin and eosin. × 39.)

tension or there may be some individual susceptibility in the blood-vessels. A similar failure to develop renal vascular lesions was observed in a number of rats with very severe, sustained hypertension.

(3) We might expect lesions of this extent to cause sufficient ischæmia in the unclamped kidney to give rise to hypertension, thereby providing the second step in the vicious circle. To test this assumption the clamped kidney was removed in some 27 animals. In two-thirds of these the operation was followed by some degree of persistent hypertension. A typical example is shown in the accompanying chart. In this case hypertension persisted for twenty-one weeks after removing the clamped kidney.

It appears, therefore, that the hypertensive lesions in the unclamped kidney were themselves capable of causing a sustained hypertension.

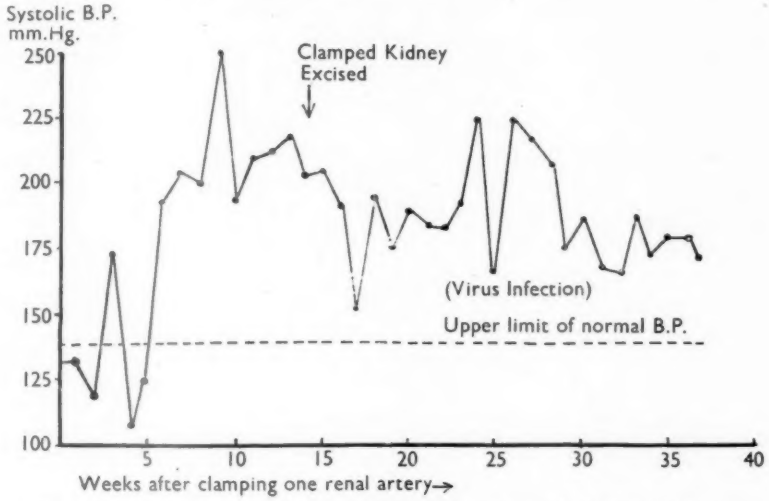


Chart to show persistent hypertension after excision of clamped kidney.

(4) Lastly, to make the vicious circle complete, it follows that these animals in which the clamped kidney has been removed should eventually develop uræmia owing to progressive vascular lesions in the unclamped kidney. Our experiments were cut short by the outbreak of war and we were unable to observe this occurrence. In several animals, however, with sustained hypertension recent acute vascular lesions were found in the kidney and in other organs a considerable time after the clamped kidney was removed; this suggests that the residual hypertension is capable of producing further renal vascular lesions.

In conclusion, if this conception of a vicious circle is substantiated it will explain the rapidly progressive terminal stages both in malignant hypertension in other forms of hypertensive Bright's disease. It is a common observation that in chronic nephritis, once the blood-pressure rises over 200 mm. the patient's condition deteriorates by what may be termed "geometrical" progression. Further it will explain the confusing similarity, both clinical and histological, between the various types of hypertensive Bright's disease in their terminal stages, and finally if, as appears possible from recent work, a reliable method of reducing the blood-pressure becomes available, the existence of this vicious circle will provide a rational basis for attempting to lower the blood-pressure in these conditions.

BIBLIOGRAPHY

Byrom, F. B., and Wilson, C. (1938), *J. Physiol.*, **93**, 301.
Goldblatt, H. (1938), *J. Exper. Med.*, **67**, 809.
Volhard, F., and Fahr, T. (1914), "Die Brightsche Nierenkrankheit". Berlin.
Wilson, C., and Byrom, F. B. (1939), *Lancet* (i), 139.
Id. (1941), *Quart. J. Med.*, **34**, 65.
Wilson, C., and Pickering, G. W. (1938), *Clin. Sc.*, **3**, 343.

Professor G. W. Pickering: In the commonest form of hypertension, benign or essential hypertension, it is still uncertain whether the renal lesions are the cause or the result of raised arterial pressure. The problem of whether or not any hypertension is renal in origin will probably be solved when it is possible to demonstrate the mechanism of renal hypertension in man.

The only form of experimental hypertension closely resembling persistent hypertension in man is that produced by reducing the blood-flow to the kidney, for example by renal artery constriction (Goldblatt *et al.*, 1934). Such animals, in addition to hypertension, show cardiac hypertrophy and a normal skin circulation (Pickering and Prinzmetal, 1938*b*). If the constriction is mild, renal function may remain relatively unaffected, if severe, renal failure occurs and in such instances retinitis and arteriolar necroses in the organs are found (Goldblatt, 1938; Wilson and Pickering, 1938). Experimental renal hypertension is chemical and not nervous in origin for it can be produced in the sympathectomized animal; and by constricting the artery supplying the kidney separated of all its nervous connexions through being transplanted in the neck. Recently it has been shown by Fasciolo, Houssay and Taquini (1938) that the arterial pressure of a nephrectomized dog under chloralose anæsthesia is raised by transplanting into its neck an ischæmic kidney from a hypertensive dog, but not by transplanting a kidney from a normal dog.

The idea that hypertension might arise from the release of a pressor substance from the kidney is very old. As long ago as 1898 Tigerstedt and Bergman described the pressor action of renal extracts and the chief properties of the active substance which they named renin. Despite its discovery by a famous physiologist but four years after that of adrenaline, only Bingle and Strauss (1909) had published any clear confirmation of the existence of renin before 1936, when work began in a number of places which has subsequently demonstrated unequivocally the existence and chief properties of renin. That this substance had proved so elusive was due to its instability, to the difficulty of separating it from depressor agents, and finally to the inhibitory effect of most anæsthetics and particularly of urethane on its action (Pickering and Prinzmetal, 1938*a*). Renin has only been extracted from the cortex of the kidney and exists in large quantities in rabbit, pig, dog and cat, but only small amounts can be obtained from human kidney, and Prinzmetal and I failed to find it in sheep, horse, cow, or whale. It is a protein separating with the globulin and particularly the pseudoglobulin fraction; it is destroyed at 60° C., by strong alkali and acid; and by alcohol and acetone at room temperature though not at −10° C.; in these solvents it is insoluble. Injected intravenously into the rabbit renin produces a rather slow rise of arterial pressure which lasts for half an hour or more in the unanæsthetized animal. In the unanæsthetized rabbit it produces fairly constant responses provided that sufficient time elapses between injections for the arterial pressure to return to normal, and this fact provides a basis for biological assay. But in the anæsthetized animal repeated injections at short intervals have long been known to produce decreasing responses. Renin produces vasoconstriction in the rabbit's ear perfused with blood but not in the rabbit's ear perfused with Ringer. These curious facts have been explained by the discovery, made independently by Page and Helmer (1940*a* and *b*) and Braun-Menendez, Fasciolo, Leloir and Munoz (1940), that renin only produces vasoconstriction in the presence of a constituent of normal blood which is gradually used up when renin acts; this substance is found in the pseudoglobulin fraction of the plasma proteins. Renin reacts with this *in vitro* and produces a third substance, angiotonin or hypertensin, which on intravenous injection gives a quick rise of arterial pressure. Hypertensin is thermostable, diffusible, and soluble in alcohol and is thus totally unlike renin chemically, from which indeed it is thought to arise by the enzyme-like action of renin on a plasma precursor. Finally there is evidence that hypertensin is itself destroyed by another enzyme which is present in many tissues and in normal kidney. Thus the present view is that renin, reacting with the precursor in plasma, liberates hypertensin which is subsequently destroyed by another enzyme system. We may ask, then, whether experimental renal hypertension is due to the release of renin from the ischæmic kidney? The present evidence suggests that it is. Thus Miss Hill and I (1939) were able to produce prolonged hypertension in the anæsthetized rabbit by prolonged infusion of renin and to show that this hypertension resembled experimental renal hypertension in the normality of the ear circulation, and in the similar duration of the hypertension following the cessation of the infusion in the one case and removal of the kidney in the other. More direct evidence is the detection of abnormal quantities of what appears

to be renin in the renal vein of animals with experimental hypertension (Munoz, *et al.*, 1940; Page, 1940). Some evidence has also been presented that hypertensin may be detected in the circulating blood—but this is less convincing. Extensive assays conducted by Prinzmetal, Kelsall and myself have yet to be gathered together and analysed with regard to the renin content of the kidney in experimental hypertension.

Attempts are now being made, particularly in North and South America, to detect renin or hypertensin in blood obtained from the renal vein and the general circulation in patients with hypertension. The technique for detecting these substances is complicated and there is no wide adoption of a method of biological assay. Without further comment I would refer readers to a recent paper by Page in which he claims that hypertensin is detectable in plasma obtained from the peripheral circulation in patients suffering from benign, malignant, and nephritic hypertension.

REFERENCES

BINGLE and STRAUSS (1909), *Deutsches Arch. f. klin. Med.*, **96**, 476.
BRAUN-MENENDEZ, FASCIOLO, LELOIR, and MUNOZ (1940), *J. Physiol.*, **98**, 283.
FASCIOLO, HOUSSAY, and TAQUINI (1938), *ibid.*, **94**, 281.
GOLDBLATT (1938), *J. Exper. Med.*, **67**, 809.
GOLDBLATT, LYNCH, HANZAL, and SUMMERVILLE (1934), *ibid.*, **59**, 347.
HILL and PICKERING (1939), *Clin. Sc.*, **4**, 207.
MUNOZ, BRAUN-MENENDEZ, FASCIOLO, and LELOIR (1940), *Am. J. M. Sc.*, **200**, 608.
PAGE (1940), *J. Exper. Med.*, **72**, 301.
PAGE and HELMER (1940*a*), *ibid.*, **71**, 29.
Id. (1940*b*), *ibid.*, **71**, 495.
PICKERING and PRINZMETAL (1938*a*), *Clin. Sc.*, **3**, 211.
Id. (1938*b*), *ibid.*, **3**, 357.
TIGERSTEDT, and BERGMAN (1898), *Skandinav. Arch. f. Physiol.*, **8**, 223.
WILSON and PICKERING (1938), *Clin. Sc.*, **3**, 343.

Lieutenant-Colonel Robert Platt: I shall confine my remarks to one of the most interesting corollaries to the recent work just described, namely the question of unilateral renal disease and hypertension.

It has been known for some time that in the human subject unilateral disease of the kidney may be associated with hypertension of the malignant type. For instance, Schwartz in 1924 described three fatal cases of malignant hypertension in children. Only in one was a post-mortem examination made, and a condition of hypoplasia of the right kidney was found. This kidney weighed 6 g. and the left kidney 150 g. The left or larger kidney is said to have shown the histological changes of glomerulo-tubular nephritis, but in view of our present knowledge of the subject one wonders if those changes were really secondary to the hypertension induced by a small ischæmic kidney on the opposite side.

Ask-Upmark (1929) recorded six cases of malignant hypertension in children with unilateral renal hypoplasia, and mentions several others described in the literature. Fishberg (1939) in his monograph states that hypoplasia of one kidney is not a rare finding in a young patient who has succumbed to malignant hypertension.

Saphir and Ballinger (1940) record three cases of unilateral stenosis of the renal artery with hypertension, in two of which post-mortem revealed changes characteristic of malignant hypertension in the opposite kidney. Thus has Nature imitated the experiments of Wilson and Byrom (1939).

The commonest pathogeny of hypertension and unilateral renal disease is either hypoplasia of one kidney or unilateral pyelonephritis. Weiss and Parker (1939) record several examples of the latter type but the two conditions often co-exist, as the hypoplastic kidney appears to be especially liable to infection.

In actual fact the underlying cause of the hyperplasia may be lack of blood supply owing to a congenitally small renal artery, in which case the hypoplastic kidney will of necessity be also an ischæmic one and therefore a potential cause of hypertension.

Since the work of Goldblatt *et al.* (1934), clinicians interested in renal disease have been on the look-out for cases of hypertension with evidence of unilateral pathology in the hope of restoring the blood-pressure to normal by removal of the faulty kidney. The first successful case was that of Butler (1937). This was a boy of 7 who developed a unilateral pyelonephritis following the removal of a renal calculus. The blood-pressure, which was normal at first, gradually rose to 160/105 and at the age of 8 nephrectomy was performed. The blood-pressure fell to 100/70 and the urinary infection cleared up.

Twenty months after operation the blood-pressure was 115/75 and the child remained well. In 1938, Leadbetter and Burkland recorded the case of a boy of 5½ with an ectopic hypoplastic kidney. He had been known to have hypertension for five years, that is since he was 6 months old. The blood-pressure fell after nephrectomy to 125/72 and later came down to 96/70. On examination of the kidney after its removal, a plug of smooth muscle tissue was found partially occluding the main renal artery.

Barney and Suby (1939) record a successful nephrectomy in a girl of 10. For two years she had had pyuria, and intravenous pyelography showed a functionless right kidney. The blood-pressure, which was 190/120, came down to 110/70 within twenty-four hours of the operation. The affected kidney was atrophied, probably as the result of healed pyelonephritis, and showed thickening of its arterioles. Twenty-one months after operation the blood-pressure was 92/60.

Striking though they are, none of these three cases showed the changes of malignant hypertension, and if the results are to be successful it is obviously important to perform the nephrectomy if possible before the onset of the malignant phase, because as Wilson and Byrom (1941) have shown, the vicious circle will sooner or later appear, with secondary changes in the opposite kidney.

Nevertheless, some successful cases have now been recorded in which nephrectomy was performed at apparently a late stage of the disease.

Boyd and Lewis (1938) describe the case of a man of 31 with headache and blurred vision; blood-pressure 200/120, retinal œdema and macular exudate. In this case a large infarct was discovered in the right kidney and after nephrectomy the blood-pressure returned to normal and the eye symptoms cleared up. The blood-pressure is known to have remained normal for six months.

Schroeder and Fish (1940) and Nesbit and Ratliff in the same year record a number of adult cases of hypertension in whom nephrectomy had been performed for various reasons. Most of these cases were not completely successful though improvement in the blood-pressure was often observed. Sometimes the results were only temporary. In many of these cases there was evidence of disease in the opposite kidney and so their suitability for operation may be questioned. Patch *et al.* (1940) have recently reported another case and collected altogether 23 in the literature.

My own case is a little girl of 8 who came to see me on May 22, 1941. The complaint was of severe headache and vomiting which had been troubling her for over six months. Recently the vomiting had been persistent every morning on waking. The previous history was important. A year before, she was investigated rather thoroughly for recurrent pyrexia. A *Bacillus coli* infection of the urine was found and an intravenous pyelogram had been performed which showed a functionless left kidney. The right kidney appeared to be normal. This was confirmed by cystoscopy and injection of indigo-carmine. Retrograde pyelography had failed to outline the left renal pelvis, the iodide solution flowed straight back along the ureteric catheter. There was no note of the blood-pressure at that time. My examination, which was just twelve months after this investigation, revealed a blood-pressure of 200/120. The heart was somewhat enlarged. Neither kidney was palpable. Both fundi showed papillœdema with advanced retinitis. The blood non-protein nitrogen was 52·3 mg. per 100 c.c. The urine—an early morning specimen—showed specific gravity 1010. Trace of albumin. No pus or casts.

An interesting feature of the case was that four times during the last few months she had had attacks of facial palsy, and when I saw her there was an incomplete paralysis of lower motor neurone type on both sides.

On May 29 she was admitted to a nursing home. The blood-pressure was then 220/120. My colleague, Mr. Nutt, reported that there were 2 dioptres of swelling in each disc, with small hæmorrhages, a good deal of retinal œdema, and some powdery white exudate around the maculæ.

The following morning Mr. Lytle did a cystoscopic examination which showed that indigo-carmine was still excreted by the right kidney within five minutes, though none at all came from the left. An anæsthetic was therefore administered and an incision made to expose the left kidney. A small hypoplastic kidney about 1½ in. in length was removed. At the end of the operation the blood-pressure was 190/120. That was at 1 p.m. At 5 p.m. the pressure was 160/128 although there was no shock or vomiting from the operation. The next day it was 155/95. The diastolic pressures throughout were difficult to take as the sounds were very faint. The blood-pressure remained at about this level—sometimes as low as 145 until the child was discharged ten days after

the operation. She was then apparently well and had had no headache or vomiting since the operation. Mr. Nutt reported that the retinal œdema was already improved. The blood non-protein nitrogen was 37·2 mg. per 100 c.c. and the urine still contained a trace of albumin.

Macro- and microscopic examination of the specimen showed evidence of chronic healed pyelonephritis in a congenitally hypoplastic kidney. There are apparently four very small arteries running into the hilum of the kidney, with no sign of a main arterial trunk. There is gross hypertrophy of the ureter. There are patches of atrophy with fibrosis of glomeruli, colloid casts in the tubules and endarteritis obliterans. Other (small) areas are apparently healthy. There is little evidence of the effects of hypertension, as one would expect. These may, of course, be present in the opposite kidney which we have not been able to examine.

She was seen again on July 30, two months after the operation. She was then apparently quite well and had had no return of symptoms. Her complexion and colouring, which had previously been sallow and unhealthy, were strikingly altered. The facial palsy had improved. The blood-pressure was 140/90. The retinal picture was much improved although there was still a little œdema of the upper and inner part of the right disc.

When again examined on October 15, four and a half months after operation, she was in excellent health. Her parents say she gets up in the morning singing instead of vomiting. She never refuses breakfast, and has no headache. Blood-pressure now 125/70, the sounds being much clearer and the diastolic pressure definite. The facial palsy is much improved. Urine Sp. Gr. 1018. No albumin. No pus or casts. The retina presents an extraordinary picture. The vessels appear quite normal, there is no swelling of the discs or œdema of the retina; yet there are extensive shining-white exudates, obviously not of recent origin, the only remaining indication of her extremely serious condition a few months ago which, but for the operation, would I am sure already have proved fatal.

REFERENCES

Ask-Upmark, E. (1929), *Acta path. et microbiol. Scandinav.*, **6**, 383.
Barney, J. D., and Suby, H. I. (1939), *New England J. Med.*, **220**, 744.
Boyd, C. H., and Lewis, L. G. (1938), *J. Urol.*, **39**, 627.
Butler, A. M. (1937), *J. Clin. Investigation*, **16**, 889.
Fishberg, A. M. (1939), "Hypertension and Nephritis". Philadelphia.
Goldblatt, H., Lynch, J., Hanzal, R. F., and Summerville, W. W. (1934), *J. Exper. Med.*, **59**, 347.
Leadbetter, W. F., and Burkland, C. E. (1938), *J. Urol.*, **39**, 611.
Nesbit, R. M., and Ratliff, R. K. (1940), *ibid.*, **43**, 427.
Patch, F. S., Rhea, L. J., and Codnere, J. T. (1940), *Canad. M. A. J.*, **43**, 419.
Saphir, O., and Ballinger, J. (1940), *Arch. Int. Med.*, **66**, 541.
Schroeder, H. A., and Fish, G. W. (1940), *Am. J. M. Sc.*, **199**, 601.
Schwartz, H. (1924), *Am. J. Dis. Child.*, **27**, 233.
Weiss, S., and Parker, F. J. (1939), *Medicine*, **18**, 221.
Wilson, C., and Byrom, F. B. (1939), *Lancet* (i), 136.
Id. (1941), *Quart. J. Med.* (New Series), **10**, 65.

Dr. Geoffrey Evans showed in the form of a graph blood-pressure readings taken regularly over a period of nineteen years of a case of benign hypertension. The patient first consulted Dr. Evans in 1922 on account of his having been told that he was suffering from high blood-pressure, and was unfit to occupy an important position in his company on that account. His blood-pressure at that time was 190/116. During the succeeding nineteen years the man had occupied the position of managing director of a large company for twelve years and afterwards became chairman of the company. During these years he had four hypertensive attacks, two of which were subacute and were controlled by conservative treatment, two attacks were acute and were controlled by intensive treatment. The highest blood-pressure readings in the acute attacks were 220/116 in one attack and 220/130 in the other. The last readings were 176/90, and these figures were the lowest for the past eight years.

Dr. Evans emphasized the importance of knowing the natural history of benign hypertension, and described four types of the condition. This case illustrated the type in which there is persistent hypertension with short phases of exacerbation and long periods of remission. He suggested that a phase of hypertension is the clinical counterpart of a

pathological state which he called arteriolosclerotic disease. He suggested that if such a phase of active disease is not controlled it may develop into so-called malignant hypertension. In such a case as that recorded he suggested that the development of recurrent hypertension was comparable to an attack of congestive heart failure in chronic myocardial disease.

Dr. Wilfrid Oakley: During an investigation on the sedimentation rate in renal disease, it was found that normal readings were obtained in cases of benign essential hypertension, but that in malignant, the sedimentation rate was definitely increased. In one case in a child in which a benign stage developed into the malignant, a change in sedimentation rate was noted, but it could not be concluded that this preceded such clinical evidence as hypertensive retinopathy.

Professor R. V. Christie: Professor Pickering has mentioned that extracts of kidney have been used in the treatment of hypertension, and I should like to ask him his opinion of the therapeutic results obtained. Both Page [1] and Grollman [2] and their co-workers have claimed results which are quite spectacular.

REFERENCES

1 PAGE, HELMER, KOHLSTAEDT, FOUTS, P. J., and KEMPF, G. F. (1941), *J. Exper. Med.*, **73**, 7.

2 GROLLMAN, A., WILLIAMS, J. R., Jr., and HARRISON, T. R. (1940), *J. Biol. Chem.*, **134**, 115.

Professor Pickering (in reply to Professor Christie): I am not entirely convinced by the evidence submitted and prefer to reserve judgment on this extremely important question.

Professor H. P. Himsworth: Whenever the results of experimental investigations appear to have a clinical bearing there will not be wanting zealous clinicians who will claim to have discovered the clinical counterparts of these experiments. The modern views on the role of chronic unilateral pyelonephritis in producing hypertension are perhaps another example of such uncritical zeal. The view is now widely publicized that chronic urinary infections often produce infection of one kidney, that the inflammatory process in this kidney affects the renal vessels so as to diminish the blood supply to that organ, and that the resulting renal ischæmia leads to hypertension. Proof of the correctness of this hypothesis appears to be lacking and the theses published in its support seem, in many instances, to be little more than circular arguments. Examination of material from cases of unilateral chronic pyelonephritis reveals that in a large number of these cases there exists some gross abnormality of the renal vessels which might well in itself lead to renal ischæmia. Lieut.-Colonel Platt's patient is a case in point; the affected kidney was supplied by four renal arteries, and it is quite usual in cases of so-called "hypertension due to unilateral chronic pyelonephritis" to find hypoplasia of the renal artery, or partial obstruction of the renal artery by an atheromatous plaque or some similar lesion which will mechanically reduce the renal blood-flow. An explanation, at least as tenable as that now fashionable, is that the primary defect in these cases is a vascular lesion causing renal ischæmia which in turn causes, not only hypertension but a diminished rate of urine formation in the affected kidney; that the consequent relative stasis in urine flow favours the occurrence of urinary infection in the renal tract of the affected side, and that as a result unilateral chronic pyelonephritis is established. This view has, incidentally, the merit of providing a reasonable explanation of the fact that the pyelonephritis in these cases is unilateral.

Dr. Paul Wood reported the result of an experiment in which a pint of blood was removed from the renal vein of a man of 21 with malignant hypertension, and transfused into an anæmic boy aged 8. No rise of blood-pressure in the boy could be detected. Details of this observation will be published in due course.

Dr. Horace Evans: Malignant hypertension as we understand it is a disease which manifests itself suddenly, usually without any indication of pre-existing high-blood-pressure, and indeed may occur in relatively young people. Although a malignant type of termination is sometimes seen after years of benign hypertension, this is rare, and it would therefore surprise me very much if this occurred in Dr. Geoffrey Evans' patient.

In regard to the association between the contracted kidney and hypertension, I have always found it difficult to understand the state of affairs as it exists in most cases of renal rickets. These patients have hypoplastic fibrotic kidneys, but there is really no hypertension.

Section of Surgery

President—E. Rock Carling, F.R.C.S.

[*December* 3, 1941]

DISCUSSION ON THE EFFECTS ON THE KIDNEY OF TRAUMA TO PARTS OTHER THAN THE URINARY TRACT, INCLUDING CRUSH SYNDROME

Dr. E. G. L. Bywaters: Impairment of urinary excretory function after severe injuries is not uncommon, but little is known about how it is produced. It seems likely that several different mechanisms are involved; with more complete investigation of these cases, it may be possible to sort them into several classes, each group depending on the particular type of functional lesion involved and on the particular ætiological agent (Table I).

Table I.—Impairment of Renal Function after Trauma to Distal Parts.

A. *Functional azotæmia* due to decreased glomerular filtration or increase in formation of waste products.

Examples: Oligæmic shock, including hæmorrhage.
Dehydration or electrolyte loss.
Pericardial tamponade and vascular stasis.

B. *Organic changes.*

Examples: Crushing injury, burns, some types of obstetric shock, traumatic liver necrosis, intravascular hæmolysis, tubular or ureteric blockage due to sulphapyridine.

After severe traumata with hæmorrhage and laceration, including those inflicted by the surgeon, oliguria is usually noted; this may sometimes be accompanied by a faint trace of albumin and hyaline casts in the urine and, more rarely, by a small rise in blood-urea concentration. This type I have classified as functional impairment of excretion, because renal tubular function itself is seldom, if ever, permanently affected; complete recovery ensues. A similar type of functional impairment, that following gastro-intestinal hæmorrhage, first observed in 1934 by Sanguinetti, has received much critical attention recently; there appear to be at least four factors involved.

(*a*) Increased protein breakdown in the small gut gives rise to increased urea formation in the liver [14]: this increase depends directly on the rate of amino-acid absorption and on adequate de-amination by the liver.

(*b*) External hæmorrhage itself, according to Black, working on dogs [3], does produce a very slight impairment of excretory function, as shown by the delayed excretion of ingested urea. This is probably due to diminished blood flow resulting from decreased

blood volume. In addition, dehydration and electrolyte loss due to vomiting, which is not an infrequent clinical complication, will further reduce excretory power owing, perhaps, to a similar decreased renal blood flow. Davis [10] has shown a non-protein nitrogen rise of about 100% following anhydræmia in dogs produced by subcutaneous injection of 25% saline.

(*c*) Decreased renal reserve may be a factor particularly in the elderly: Wallace and Schafer [21] have shown that, after venesection of a litre of blood, the blood urea rises only in patients with hypertension and renal sclerosis.

(*d*) The oliguria accompanying the systolic pressures below that necessary for glomerular filtration to occur may produce a more lasting effect on the kidneys, as is recorded by Stafford [20], after a stab wound of the heart, where pericardial tamponade developed and the blood pressure remained at or below 60 mm.Hg for fifteen hours; there was oliguria for eight days, with blood casts and albumin, a blood urea rising to 220, hypertension and an excretory function, measured by serial phenol-red excretion tests, temporarily decreased to zero.

These four factors, increased protein breakdown, decreased renal blood flow, decreased filtration pressure, and decreased renal reserve, may all possibly play some part in actual clinical cases, both of gastro-intestinal hæmorrhage and also following trauma. Generally, the renal lesion is functional and not structural.

As elsewhere, however, there is no sharp dividing line between functional and organic change except on paper (Table I). Structural changes are sometimes seen following burns (although even in severe cases it sometimes happens that neither functional nor organic change is found), in some types of obstetric shock (Young and McMichael, 1941 [22]) after septic abortions (Bratton, 1941 [4]) and in the so-called "hepato-renal syndrome" described after traumatic liver necrosis (Furtwaengler, 1927 [12]). I am not discussing either these or the anuria sometimes seen in cases of severe trauma due to sulphapyridine blockage or mismatched transfusion, because I want chiefly to deal with "crushing injury". The Medical Research Council has collected details now of over 70 cases; it is on this group that the following remarks are based.

It was not until after the first cases had been published that we discovered that this "new" syndrome, occurring in patients pinned for hours under the debris of bombed houses, was not new at all. It was recognized in Germany during the 1914-1918 war [11], mentioned in official books on military surgery [15], and worked up pathologically [19]; indeed, it had only been missed by a week in 1909 following the Messina earthquake: there, the German relief hospital arrived on the fourteenth day and observed only the muscle and skin gangrene in recovering cases [9]. Why it has not been remarked on since 1923, or at all in Anglo-Saxon literature, would, perhaps, be understandable if it occurred only with bombs and in earthquakes, but it does occur in civil practice following mining accidents, as McClelland has recently recorded from Canada [17], and also, as will be detailed later, following traumatic injuries to main vessels.

Clinical Account

A typical severe case, having a history of being buried for several hours with masonry resting across a limb, will be shocked on admission or soon after, with a fall in blood-pressure following a preliminary period of apparent well-being. During this initial phase, hæmoconcentration occurs (and compensatory vasoconstriction) from loss of plasma into the injured part, which becomes swollen and hard. There is also loss of sensation and power and the skin shows whealing and, later, blisters: arterial pulsation distally may be impaired. After restoration of blood volume by transfusion of blood or serum, the patient recovers, but it is noticed that the urine is blood-stained and contains albumin and pigmented granular casts. In the next few days the urinary output decreases and becomes clearer: the blood-pressure rises to a high level: there is a progressive increase of blood urea, phosphate and potassium, and a decrease in alkali reserve. The patient becomes alternately drowsy and apprehensive: death occurs suddenly about the seventh day, and is occasionally preceded by abnormalities of cardiac action similar to those produced experimentally by potassium intoxication.

An increasing number of mild and surviving cases are being recognized and published, often as showing the beneficial results of treatment. Most of these show no clinical (hypotensive) "shock", but this is not to say they are not shocked, as may be illustrated

by fig. 1, a case which I saw through the kindness of Mr. Riddell and Dr. Dow at St. George's Hospital. The patient showed no pallor or sweating or fall of blood-pressure, yet, as calculated by venous hæmoglobin and hæmatocrit readings, she had lost over a litre of plasma into the tissues, without either external hæmorrhage or any more œdema than a few square inches over one hip; she passed myohæmoglobin in the urine with casts. Probably many cases go through this first phase of shock without its being noticed. That this was a case of "crush syndrome" was established by the finding of myohæmoglobin and creatine in the urine, sure indices of muscle damage, and by the presence of albumin and casts, with a depressed urinary urea concentration and azotæmia, pointing to parenchymatous renal damage.

The two most interesting biochemical features in our own cases were those relating to renal function and those relating to tissue breakdown. For the former, comparison of

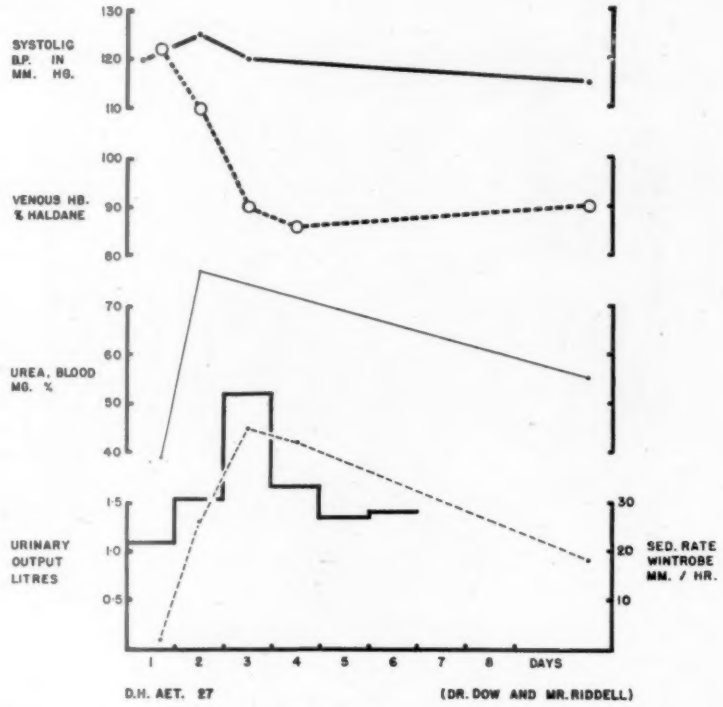


FIG. 1.—Mild case of crushing injury.

Note hæmoconcentration on entry, with normal blood-pressure, and rise in urine output, blood urea and sedimentation rate. She showed myohæmoglobinuria and creatinuria with a urinary pH of 4·6, responding rapidly to alkali therapy.

blood and urinary figures showed that tubular function was impaired, there being failure to concentrate urea and failure to reabsorb chloride: in addition, there was leakage of glomerular filtrate back into the blood-stream. There may be biochemical evidence of recovery of renal function, even though death occurs at the usual time (seventh day) and in the usual way [2]. Secondly, there was creatinuria and myohæmoglobinuria [6], which must have come from damaged muscle: this tissue autolysis probably explains also the

acidosis and the very low urinary pH almost invariably seen as soon as circulation to the damaged part is re-established. Whether the phosphate and potassium increases can in part be thus explained, is still uncertain.

Pathological Features

If death does not occur before the usual time from other causes, the kidneys are swollen and wet. The most obvious feature microscopically is the presence of pigment casts in the collecting tubules similar to those seen in the urine. More important, we think [7], is the severe tubular damage seen in the distal convoluted tubules and Henle's loop of the boundary zone—often with complete necrosis—and discharge of hyaline casts into the interstitial tissue and surrounding cellular reaction (fig. 2). This corresponds with the biochemical indication of tubular dysfunction and leakage.

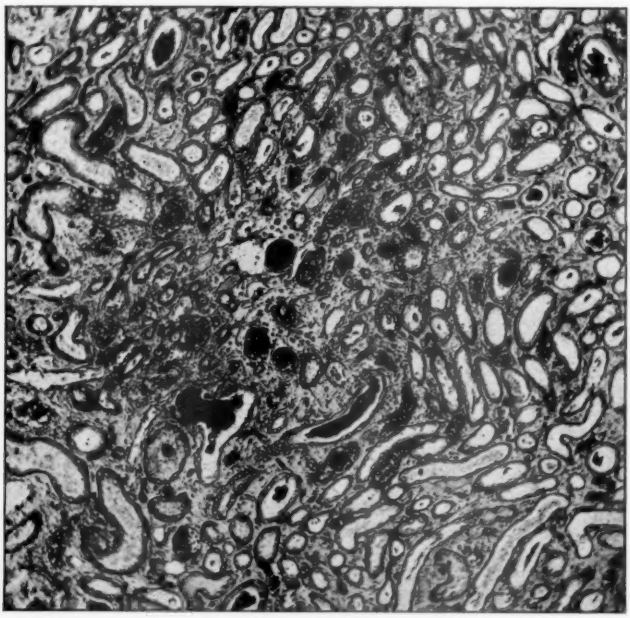


Fig. 2.—Boundary zone from D.W. (× 80, Macgregor's Azan Carmine) showing focal area of necrosis, and on its margin, the extrusion of hyaline cast into œdematous interstitial tissue from partially necrotic tubule.

This histological change is not entirely specific, since we have seen a very similar picture in kidneys from some wasting conditions, from a case of paralytic myohæmoglobinuria and from mismatched transfusion. However, the pigment excreted in the urine in these cases is not hæmoglobin but myohæmoglobin, whose renal clearance is twenty-five times that of hæmoglobin, thus accounting for the lack of plasma colour and the absence of jaundice. It may be distinguished in the Hartridge reversion spectroscope by the different position of the bands.

Myohæmoglobin, along with other autolytic products, comes from muscle, which shows necrosis, loss of staining ability, and reactive changes such as cellular increase, œdema and calcification. There are three main types of muscle lesion:

(1) Part only of the muscle is necrotic, and there is a sharp boundary line between living and dead, corresponding exactly with the pressure marks seen on the skin. This is the commonest type of change, and, we think, is due to direct pressure ischæmia.

(2) In other cases, the whole muscle may be necrotic, irrespective of skin pressure areas. These are muscles contained within tight fascial sheaths, and it seems probable that rise of intrafascial pressure may be responsible for the ischæmic necrosis seen.

(3) Finally, in occasional cases, isolated fibres show necrosis. This is shown in our own Case I [5], where we believe the ischæmia was in large degree vasospastic in origin, due to perivascular hæmatoma. Cohen [8], has recently emphasized this possibility. This type of case may be characterized by lack of progressive swelling of the leg, and by little in the way of hæmoconcentration. The same isolated fibre necrosis is seen, too, in cases with arterial rupture and limb ischæmia, without any prolonged crush, such as may occur after an automobile accident (fig. 3). These cases, of which seven have been recently recognized, as well as the two originally recorded by Husfeldt and Bjering [13], closely resemble cases of crushing injury clinically, biochemically and histologically, as will be brought out later in the discussion, but (except for a forty-five-minute crush case of Mr. Belsey and Dr. Miles, where we were able to identify myohæmoglobin) it is still uncertain, in this type of case, which has often received massive blood transfusions, whether the

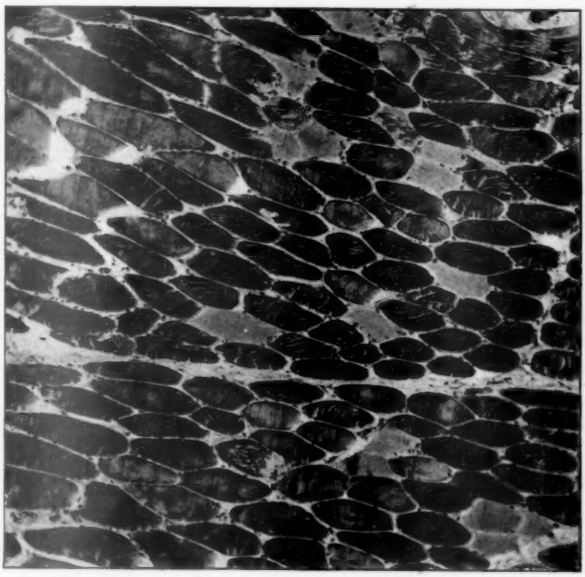


FIG. 3.—Muscle from ischæmic limb below site of rupture of popliteal artery (Mr. Graham's case) showing loss of staining ability and early vacuolation (× 80, hæmatoxylin and eosin).

pigment excreted in the urine is hæmoglobin or myohæmoglobin; it is often obviously a very important point. Such cases must occur frequently, and it is to be hoped that with the knowledge gained from the four cases described later, they will be more frequently recognized and investigated (*see* figs. 6, 7, and 8).

In any given case of crushing injury, then, there may be ischæmic muscle necrosis due to any or all of these processes.

PATHOGENESIS

Although muscle ischæmia and necrosis are thought to play important parts in the genesis of the renal lesion, it is still uncertain how they act. Obstruction of tubules by

casts containing myohæmoglobin derivatives certainly occurs, especially in acid urine as Baker and Dodds [1] pointed out for hæmoglobin, but there may be in addition another factor concerned in the formation of the casts, either of a toxic nature producing catarrh of the lining epithelium, or some such factors as decreased urine flow due to shock, or endocrine disturbances, to cite only two possibilities. Furthermore, obstruction by casts must be widespread to be effective, and what urine is secreted would be of normal composition. It seems, therefore, to us that another mechanism besides obstruction must be involved, perhaps a toxic process producing epithelial necrosis, perhaps tubular ischæmia due to the rise in intrarenal pressure consequent on obstruction, perhaps something else. Professor Shaw Dunn has previously drawn attention to the similarity of the necrosis produced experimentally by phosphate (which is increased in the blood in these cases). Experimental work in progress on dogs by Professor Winton and his associates, and on rabbits at the Postgraduate Medical School indicates that there is at least one other factor necessary besides tubular blockage. Thus the pathogenesis of this condition is still as much a matter of speculation as the similar problem of renal failure following mismatched transfusion.

Prognosis

The critical period is towards the end of the first week; most cases lasting to the eighth or ninth day will recover. The surviving cases (which amount to about one-third of the total collected) have been, in general, less severely injured than the fatal cases. The severity of the injury must be judged by the amount of tissue rendered necrotic, and hence, when the circulation is re-established, by the amount of hæmoconcentration produced by loss of plasma into the damaged area. The severity of the renal lesion must be judged by the rise in blood urea and blood-pressure, by the urinary output, and by tubular function as measured by the percentage concentration of urinary urea compared with that in the blood. A good prognosis may be given with small injuries, and a relatively good one with injuries so severe that there is no re-establishment of the circulation to the part. A good prognosis may be given with a falling blood-urea level or, since there is a progressive rise in most fatal cases, a blood-urea figure below the expected level for the time after injury. To illustrate this, in fig. 4 I have charted blood-urea levels from 16 patients (data sent to the Medical Research Council through the kindness of the physicians and surgeons concerned). The fatal cases show a straight line curve rising steadily to death on or about the seventh day. The surviving cases (circles) may follow this curve and then fall, or they may fail to rise as much and fall earlier. The fall is associated with a diuresis, as is shown in fig. 5 (where five recovering cases are contrasted with the case recorded in the original publication [2] which died). At the same time the hypertension disappears. There is as yet no absolute proof that prognosis as regards renal failure depends on the treatment administered, since not only is prognosis at the beginning of treatment uncertain, which invalidates many of the "success" claims, but treatment is seldom adequate or begun early enough, and this invalidates most of the conclusions regarding failure. However, it appears probable that renal damage is produced as soon as absorption of autolytic products from the limb occurs, that is along with the re-establishment of the circulation. This is the critical time: unless the kidneys are adequately protected, perhaps by diuretics such as fluids by mouth or vein and sodium sulphate, perhaps by alkali, it seems possible that measures directed towards increasing the circulation to a necrotic limb, may do more harm than good. Casualties rescued from collapsed houses have usually been first treated for shock, then the circulation to the injured limb has been re-established and the kidneys have not been considered until the fourth day, but—if instead of this procedure, these cases were first of all treated for renal failure, then a good alkaline diuresis established as soon and as rapidly as possible, and finally the shock and local lesion treated—I think the mortality figures would improve. Prophylactic fluid intake during a raid is, of course, an individual affair, but one of Dr. Grant's cases who recovered had had two pints of beer just before burial.

In conclusion, I want to re-emphasize that we know very little as yet about the syndrome; further accurate and detailed observations relating to renal function are urgently needed both in this type of injury (particularly of that period immediately before and after release from the debris) and also in various other types of trauma.

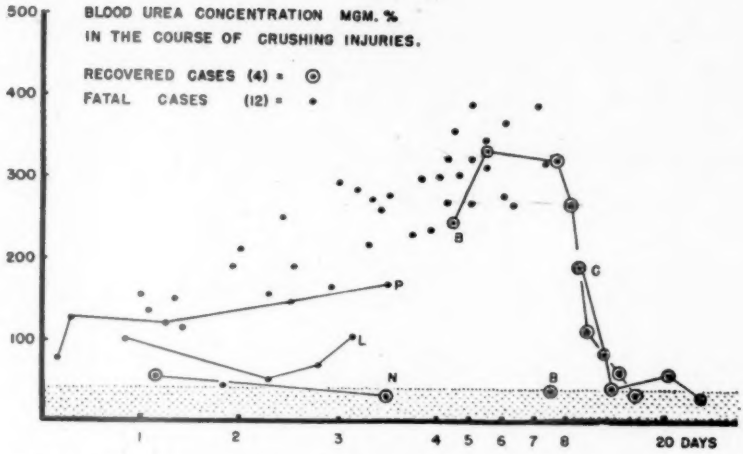


FIG. 4.—Blood-urea concentration in crushing injury. Composite chart, using data previously recorded (*Brit. M. J.*, 1941 (i), 427, and (ii), 475, *London Hospital Gazette*, June 1941, 44, 126) as well as hitherto unpublished cases through the kindness of Dr. Warner and Dr. Horn.
Dr. Pochin's figures (P) are of non-protein nitrogen (mg.%).

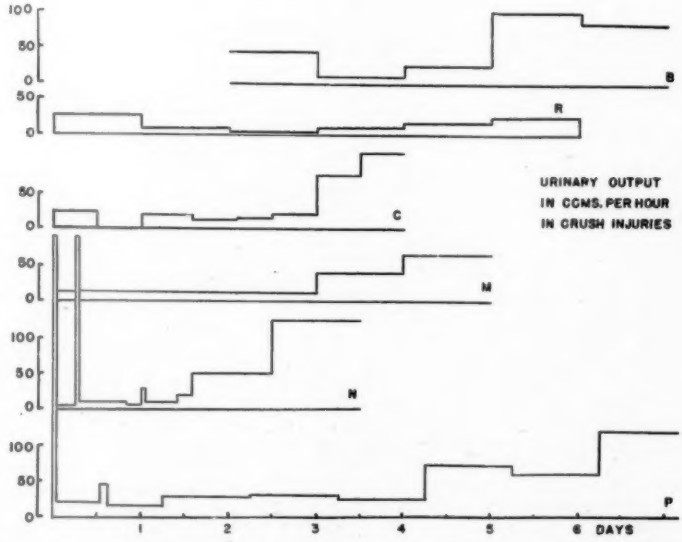


FIG. 5.—Urinary output in crush injury. 5 recovered cases, N., M., C., B., and P. (data respectively supplied by Mr. Neligan and Professor Ellis, Mr. Naunton Morgan, Professor Christie, Mr. Blackburn and Dr. Kay and Dr. Pochin) and one fatal case, Mr. Romani's (R).

BIBLIOGRAPHY

1 BAKER, S., and DODDS, E. C. (1925), *Brit. J. Exper. Path.*, **6**, 247.
2 BEALL, D., BYWATERS, E. G. L., BELSEY, R. H. R., and MILES, J. A. R., *Brit. M. J.* (i), 432.
3 BLACK, D. A. K. (1940), *Lancet* (ii), 345.
4 BRATTON, A. (1941), *ibid.* (i), 345.
5 BYWATERS, E. G. L., and BEALL, D. (1941), *Brit. M. J.* (i), 427.
6 BYWATERS, E. G. L., DELORY, G. E., RIMINGTON, C., and SMILES, E. (1941), *Biochem. J.*, **35**, 1164.
7 BYWATERS, E. G. L., and DIBLE, J. H. (1942), *J. Path. & Bact.*, **54**, 111.
8 COHEN, S. M. (1941), *Guy's Hosp. Rep.*, **90**, 201.
9 COLMERS, V. (1909), *Arch. f. klin. Chir.*, **90**, 701.
10 DAVIS, H. A. (1940), *Proc. Soc. Exper. Biol. & Med.*, **43**, 357.
11 FRANKENTHAL, L. (1916), *Virchow's Arch. f. Path. Anat.*, **222**, 332.
12 FURTWAENGLER, A. (1927), *Krankheitsforschung*, **4**, 349.
13 HUSFELDT, E., and BJERING, T. (1937), *Acta Med. Scandinav.*, **91**, 279.
14 JOHNSON, J. B. (1941), *J. Clin. Investigation*, **20**, 161.
15 KAYZER, F. F. O. (1922), In Von Schjerning's "Handbuch der Arztlichen Erfahrungen im Welte-Kriege", **1**, 36.
16 MAYON-WHITE, R., and SOLANDT, O. M. (1941), *Brit. M. J.* (i), 434.
17 MCCLELLAND, J. (1941), *Canad. M. A. J.*, **45**, 332.
18 M. R. C. Sub-Committee on Traumatic Œdema (1941), *Brit. M. J.* (i), 449.
19 MINAMI (1923), *Virchow's Arch.*, **245**, 247.
20 STAFFORD, E. S. (1940), *J. Thoracic Surg.*, **9**, 652.
21 WALLACE, J., and SCHAFER, E. P. S. (1941), *Lancet* (ii), 393.
22 YOUNG, J., and MCMICHAEL, J. (1941), *Brit. M. J.* (ii), 887.

Mr. Ronald Belsey: Only by detailed observation, recorded at the bedside, and not from memory when the excitement has evaporated, shall we obtain the vital pathological data without which there can be no rational approach to the problem of treatment. When several hundred cases of this condition have been fully investigated, clinically and biochemically, then will be the time to get dogmatic about treatment. For the present let our attention be directed to the problem of deciding what the surgeon is trying to do, rather than how he is going to do it.

In the crushed limb the following changes have been observed: First, necrosis of muscle, patchy in distribution and rarely corresponding to areas of damaged overlying skin such as would suggest that the necrosis is due to direct pressure. The muscle is pale and mottled. Hæmorrhage into the muscle or tissue planes is not constant. There is œdema of the limb and an increase of tension in the tissues within the fascial compartments of the limb. During life there is frequently evidence of impaired peripheral circulation and sometimes absent pulsation, but at autopsy there is rarely evidence of thrombosis or gross damage to the main arteries of the limb, although in a few instances rupture of a major vessel has been found. Thrombosis and mural necrosis have been demonstrated in some of the smaller muscular arterioles, and in the veins. Intense arterial spasm would appear to be the common cause of the ischæmia and has been demonstrated at operation. Clinically, peripheral arterial pulsation is sometimes absent when the case is first seen; in other cases an initially weak pulse becomes progressively obliterated with increasing œdema of the limb during the first day or two. But in at least two recorded cases the pulse has been normal, and in one was always stronger than in the uninjured limb.

Loss of nerve function has been recorded in the majority of cases, and has commonly involved all the nerves of the limb, a distribution suggesting that the failure of conduction is due to ischæmia and asphyxia rather than direct pressure. In the cases that have survived the recovery of nerve function has been steadily progressive over a period of six to twelve weeks, and usually complete.

Simple fractures may be present, but evidence of gross trauma to the limb is remarkable by its absence. The overlying skin seldom shows more than slight grazing initially, but with the increasing œdema may show bleb formation in places where there has never been any evidence of direct bruising of the skin.

So much for the facts already observed, on the basis of which we assume that there occurs in the crushed limb ischæmic necrosis of muscle, due probably to traumatic arterial spasm, possibly to direct pressure also; that with restoration of the blood supply to the limb there occurs a flooding of the circulation with a hypothetical toxin, and an outpouring of fluid into the tissues of the limb from vessels rendered abnormally perme-

able by asphyxia, and resulting in an increase in subfascial tension which may be complicated by a recurrence of the vascular spasm.

We do not yet know: (1) How long a period of ischæmia or pressure is necessary to produce the changes in muscle that are interpreted as necrosis. The average period of burial or crushing has been about eight hours, but we have recently seen a case in which the patient was trapped for only forty-five minutes at most; a reflex vascular spasm may have been active for a much longer period following the patient's release; (2) whether toxin production continues after restoration of limb circulation, and whether it is influenced by the metabolic activity of the tissues; (3) at which stage the renal damage occurs, whether it is an early irreversible change, or whether progressive damage takes place during the period of survival of the patient; (4) if muscle necrosis is the sole cause of the renal damage.

The search for collateral evidence that might throw light on the pathology of the crushed limb, and point the direction in which the therapeutic solution lies, has been without success.

In Volkmann's contracture we have a condition of acute muscle necrosis, in which, according to Griffiths, there is evidence that the ischæmia is due to vascular spasm. Whether the resulting changes in muscle are comparable to those occurring in crushed limbs remains to be demonstrated, but as yet we have been unable to find any mention of renal impairment or the changes in clinical condition that accompany the latter injury. Granted that the volume of muscle involved in the typical Volkmann complicating injuries to the elbow is small, it is conceivable that minor degrees of renal impairment may have failed to attract attention.

A survey of the case records of patients with limb fractures admitted to a general hospital during the last ten years, has again elicited no reference to complications at all comparable to those under discussion.

Cohen has recently reviewed the literature on acute traumatic arterial spasm and stresses its frequency, but again the incidence of ischæmic muscle necrosis seems never to have aroused any suspicion of renal damage.

The work of Andrews on experimental uræmia has excited comment during the discussion of the crush syndrome, but with little justification. Andrews ligated the limbs of dogs for varying periods sufficiently tightly to produce œdema of the limb. Following release of constriction in animals which were receiving intravenous hypertonic saline, Andrews observed an immediate fall in the output of urine, a lowered alkali reserve and ultimately a clinical condition suggestive of uræmia, terminating in death. However, he could demonstrate only slight changes in the convoluted tubules, not extensive enough to cause blocking, and concluded that the kidneys were not responsible for the suppression of urine.

Allen ligated limbs of rats and rabbits with rubber tourniquets to stop all circulation, and observed that release after five hours was invariably followed by death of the animal from a condition he describes as "secondary shock" but does not define. The condition was temporarily relieved by transfusion with blood from normal or equally shocked animals. Death could be prevented by amputation of the limb within ninety minutes of release of the tourniquet, by the early intravenous administration of saline from the time of release, or by the refrigeration of the ischæmic limb at temperatures of 1° or 2° C. during the period of constriction. This last observation may be significant and relevant to the present discussion.

Before attempting to assess the influence of surgical treatment on the course of recorded cases of the crush syndrome it is essential that we establish certain definite criteria of diagnosis, prognosis and clinical response, and unless these criteria are conscientiously observed, no conclusions can justifiably be drawn. The problem is rendered much more difficult by the fact that several forms of treatment have been used concurrently, and as no strict attention has been paid to the chronological sequence of therapy and response, it has been impossible to determine their relationship.

In future there must be more control of and attention to the time factor. We now know that spontaneous recovery can occur, and difficulty arises from the fact that treatment, to be of any avail, will probably have to be started very early, before it becomes obvious from the rapidly diminishing urine output that the case falls into that group that inevitably dies between the sixth and ninth days with complete anuria.

If every case is adequately investigated and reported it may eventually be possible to

infer from the extent and distribution of the crush lesions whether any given case is likely to survive. The tendency to record only those cases that recover, and suppress the failures, cannot be too strongly deprecated.

There can be no excuse now for failure to foresee the advent of this state in any case of massive tissue trauma before the patient becomes uræmic.

To obtain the prognostic criteria that presage complete failure, only those cases dying with anuria or intense oliguria between the sixth and ninth days should be used. This selection of material will tend to eliminate cases dying of secondary shock with its attendant renal impairment, or later septic complications.

Little in the way of operative treatment has been employed as yet, and probably quite rightly. Primary amputation has been performed in three cases, two of which were fatal. In the first case recorded by Bywaters and Beall, a female aged 17, whose left leg had been crushed for nine hours, amputation through the thigh and apparently above the level of tissue damage was done at the thirty-sixth hour, on account of incipient gangrene of the limb. There was no evidence of damage to other limbs. Death occurred on the sixth day with almost complete suppression of urine.

Decompression of the limb by incision of the deep fascia has been done in seven cases, of which only three have been recorded so far. Three cases died and four survived. Bywaters and Beall recorded two cases: in the first, a male aged 34, with injuries to all four limbs, decompression of the left arm was performed on the second day, on account of the local condition of the limb; the hand was described as "blue, cold and pulseless". Pulsation returned following this operation. In this case the lowest recorded urine output was 20 oz., but was probably higher as incontinence was present. The blood urea rose to 345 mg.% on the seventh day, when the patient died with evidence of staphylococcal pyæmia. No change in the general condition of the patient was observed following operation.

In the next case, a male aged 16, with a crush injury of the left leg, decompression was performed on the third day owing to failure of the peripheral circulation and threatened gangrene; pulsation was restored but the patient died suddenly eight hours after operation. At autopsy the muscles of the leg showed the typical patchy necrosis, but the kidneys were not examined microscopically. This case must be rejected as far as the present survey is concerned on account of the absence of any record of the urine output or blood chemistry.

The best recorded case of survival following limb decompression is that reported from the London Hospital of a girl, aged 18, whose left leg was crushed for fourteen hours. Again we are confronted by the suspicion that this case would probably have survived without operation in view of the fact that the urine output never fell below 37½ oz. and the maximum blood urea recorded was 54 mg.%. The fate of the limb without decompression is another matter. But in the case of a girl, aged 17, buried for thirteen hours, decompression of the left thigh on the third day failed to save the limb, which was eventually amputated below the knee for gangrene. Decapsulation of the kidneys has been performed in one case with established renal failure, but the patient died.

There emerge two distinct problems: first, to save the patient's life, and secondly to save his limb. The latter problem would appear to depend upon our ability to relieve intense spasm of the peripheral arteries, the primary problem is how rapidly this can be achieved. The two aims may be mutually antagonistic in that restoration of the circulation to the crushed limb may lead to a sudden flooding of the body with toxin. The sudden unexplained collapse of Bywaters' fourth case eight hours after limb decompression may be significant in this respect.

I shall now describe five cases that have been admitted to St. Thomas's Hospital, London, and a St. Thomas's Sector Hospital. Full case reports will be published in due course.

CASE I.—A man, aged 20, has already been reported. The region of his left knee was crushed for ten hours. On admission to hospital he rapidly recovered from shock. The local damage to the left leg appeared relatively slight; the œdema was confined to the region of the knee, and pulsation in the dorsalis pedis and posterior tibial arteries was stronger than on the normal side. By the fourth day the urine output had dropped to 3 oz., the blood urea was 165 mg.%, the patient vomiting and drowsy. The urine excretion began to improve, but the blood urea rose to a maximum of 393 mg.% on the eighth day, when the patient died suddenly. Autopsy revealed muscle necrosis in the calf and lower thigh, and typical renal changes. At no time did there

appear to be any indication for surgical treatment; it would have taken a bold man to amputate the left leg through the thigh within Allen's experimental time limit of one and a half hours following release.

CASE II.—A girl, aged 18, had both legs crushed for nine hours. Shock was not severe but intense oliguria was present throughout, the maximum measure obtained being 7 oz. on the fourth day. No intravenous fluid therapy was given and for the first five days this patient received the rest and quiet, the lack of interference, that have been advocated so strongly by the non-interventionists. Clinically the patient resembled a case of terminal uræmia. The swelling of both legs was intense, peripheral pulsation was diminished but present, till the fifth day, when the pulse was hardly perceptible in the right leg. Under general anæsthesia, the right leg was decompressed from the middle of the thigh to the ankle. Œdema fluid poured from every tissue plane and the subfascial tension was very high. The femoral artery was exposed in Hunter's canal and found to be in a state of intense spasm, about 3 mm. in diameter and without visible pulsation. There was extensive muscle necrosis and contusion. The patient died suddenly with complete anuria on the next day. Oligæmia and dehydration probably contributed to the death of this patient. Unfortunately a full biochemical investigation was not possible as the hospital had just been bombed again. Amputation was out of the question in this case, and the extent of the injuries were such that no treatment would probably have been of any avail.

CASE III.—A man, aged 36, was pinned for eight hours with his right arm above his head. On admission there was localized swelling of the right arm in the region of the biceps muscle, slight swelling of the left forearm, and bilateral incomplete median and ulnar nerve lesions. The pulse was normal at both wrists. The urine showed the typical changes: blood, albumin and pigment casts. Next day the whole of the right arm was tensely swollen, the pulse had disappeared, the blood urea was 52 mg.%, but there was no oliguria. Under general anæsthesia the right arm was decompressed by slitting the fascia from the upper third of the arm to the middle of the forearm. The subfascial tension was greatly increased, all layers were œdematous and the biceps and brachialis muscles showed the typical necrotic changes. The brachial artery was identified with difficulty, owing to its intense spasm, surprisingly small size, and complete absence of pulsation. The outer coat of the vessel was dissected off for a distance of about 1 in. at a point high in the arm, the wound was left wide open, and the limb elevated on an aeroplane splint. By the time the patient had returned to the ward peripheral pulsation at the wrist was normal. Next day the blood urea rose to 68 mg.% but the urine measure was satisfactory. Albumin and pigment casts were still present. At no time did the general condition of the patient give rise to any anxiety. Secondary suture of the wound was done two weeks later and the patient made an uninterrupted recovery. Nerve function has returned and the only residual deformity is limitation of extension of the right elbow, due to fibrosis of the biceps and brachialis muscles. In this case surgical treatment was directed entirely to the preservation of the limb.

CASE IV.—Was of unusual interest and will delight the hearts of the non-interventionists. A boy, aged 14, was pinned by the shoulders and both legs below the knees for seven hours. He reports that his left arm went numb very quickly. On admission to St. Thomas's Hospital he was not considered to be shocked and was transferred to Botleys Park Hospital on the same day. There was swelling of the left arm, marked in the region of the elbow, patchy anæsthesia of the hand, wrist drop, a diminished pulse at the wrist, slight œdema of both legs below the knees and bilateral foot drop. His urine was muddy brown, contained red cells, methæmoglobin but no albumin. The general condition remained fairly good for the next four days, with a daily urine measure of about 20 oz., but there was progressive œdema of the left arm and right leg. The pulse was never obliterated. On the fifth day the patient was drowsy and began to vomit; urine output dropped to 7 oz. and the blood urea was 120. By the eighth day the general condition was poor, blood-pressure was 150/70, the urine excretion had risen to 72 oz., but the blood urea was 460 mg.% and the urea clearance 9%. From then on the patient began to recover, but as the œdema in the left arm subsided, so the muscles began to contract, flexors more than extensors, and a Volkmann type of contracture appeared imminent. By intensive physiotherapy and the use of splints at night the contractures were controlled. Four months after the injury, urea clearance was 108%, blood urea 17 mg.% but the urine still contained occasional non-pigmented hyalo-granular casts; nerve function was completely restored and the only residual disability was slight limitation of extension of the fingers of the left hand and dorsiflexion of the right foot. At no time did the urine contain any albumin.

The main interest in this case lies in the extreme degree of nitrogen retention, the almost complete recovery without specific treatment, and the fact that at one stage amputation of the arm was strongly advocated.

CASE V.—A man, aged 37, was crushed for only forty-five minutes by a falling crane in a munition factory. He sustained multiple compound fractures of the right leg, a fractured pelvis, complete rupture of the membranous urethra, and a fracture dislocation of the left ankle-joint. Shock was severe and when controlled by multiple blood transfusions, the right leg was amputated through the thigh, the wound of the left ankle excised, and a suprapubic cystostomy performed. On the second day the left leg, between ankle and knee, where previously there had been no evidence of trauma, showed all the characteristic crush changes, including bleb formation of the skin, anæsthesia, and muscle paralysis. The blood-pressure was 170/100, blood urea 209 mg.%, the urine contained pigment casts, albumin, red cells and myohæmoglobin, but the measure never dropped below 18 oz. On the third day vomiting was profuse, the patient was drowsy and the blood-pressure had risen to 200/100, the blood urea to 238 mg.%. Death occurred on the fourth day, from traumatic paralytic ileus with renal failure a contributing factor. At autopsy the muscles of the left calf were necrotic, and the kidneys showed the typical lesions in the tubules.

In this case the interest centres on the short period of forty-five minutes during which compression can have occurred. Any surgical attack on the left leg which showed the crush changes was contra-indicated by the severity of the co-existing lesions.

And so the picture yet remains far too confused to justify any conclusions upon treatment for the local condition of the crushed limb. In none of the published case reports is there evidence that operative surgical treatment has played any part in saving the life of the patient. The case for amputation remains unproved. Ablation of crushed arms is probably never indicated, but in view of the poor prognosis with extensive crushes of the leg, the application of a tourniquet to the limb before, or at the time of release, by a competent doctor attached to the rescue squad, followed by early amputation as soon as shock has been controlled, would appear to be rational. Many limbs might be sacrificed unnecessarily, and until the crush syndrome can be reproduced experimentally, and the fatal renal complications averted by early amputation, such reasoning should be applied to the case of the human being only with extreme caution.

Limb decompression is indicated as a means of saving the limb in those cases where peripheral pulsation has completely disappeared, but apparently has no influence upon the patient's general condition. The use of drugs, of which alcohol in large doses is probably the best, to relieve peripheral arterial spasm, has not been tried in this condition to my knowledge. Splintage and refrigeration of the damaged limb with ice-bags, as a method of reducing the metabolism of the limb during the period of ischæmia, and possibly also of diminishing toxin production, would appear to be rational if commenced early, in view of the experimental work of Allen, and certainly demands a carefully controlled clinical trial.

BIBLIOGRAPHY

ALLEN, F. M. (1937), *Tr. A. Am. Physicians*, **52**, 189.
Id. (1938), *Am. J. Surg.*, **41**, 192.
Id. (1938), *Surg. Gynec. & Obst.*, **67**, 746.
Id. (1938), *Ann. Surg.*, **108**, 1088.
Id. (1939), *Arch. Surg.*, **38**, 155.
Id. (1939), *Am. J. Surg.*, **45**, 459.
Id. (1939), *Surg. Gynec. & Obst.*, **68**, 1047.
ANDREWS, E. (1927), *Arch. Int. Med.*, **40**, 548.
BEALL, D., BYWATERS, E. G. L., BELSEY, R. H. R., and MILES, J. A. R. (1941), *Brit. M. J.* (i), 432.
BLACKBURN, GUY (1941), *ibid.* (ii), 475.
BYWATERS, E. G. L. (1941), *ibid.* (ii), 29.
BYWATERS, E. G. L., and BEALL, D. (1941), *ibid.* (i), 427.
BYWATERS, E. G. L., and DELORY, G. E. (1941), *Lancet* (i), 648.
DINSDALE, T. (1941), *Brit. M. J.* (i), 645.
FISHER, S. W., LLOYD, E. R., and DAVIES, F. M. E. (1941), *ibid.* (i), 534.
GILMOUR, J. R. (1941), *Lancet* (i), 524.
GRIFFITHS, D. L. (1940), *Brit. J. Surg.*, **28**, 239.
HENDERSON, R. G. (1941), *Brit. M. J.* (ii), 197.
HILL, Sir L., HARRIS, H. A., FRANKLIN, R. H., and DOUGLAS, D. M. (1941), *ibid.* (i), 491.
LONGLAND, MURRAY (1941), *Lancet* (ii), 158.
MCMICHAEL, J. (1941), *Brit. M. J.* (i), 608.
MAITLAND, A. IAN L. (1941), *Lancet* (ii), 446.

MAYON-WHITE, R., and SOLANDT, P. M. (1941), *Brit. M. J.* (i), 434.
MED. RES. COUNC. SUB-COMMITTEE ON TRAUMATIC ŒDEMA (1941), *ibid.* (i), 449.
MILLER, HUGH (1941), *ibid.* (i), 685.
PATEY, ROBERTSON (1941), *Lancet* (i), 780.
S. L. and G. K. R. (1941), *Lond. Hosp. Gaz.*, 44, 126.
WINSBURY-WHITE, H. P. (1941), *Brit. M. J.* (i), 685.

Dr. J. McMichael: We may safely disregard transfusion and bacterial toxæmia as causes of the renal failure. There is little doubt that breakdown (? autolytic) products from dead or dying muscles are the main factors. Professor Winton and his colleagues at University College have shown that two main effects are produced in the kidney by crushing injuries: (1) poisoning of tubule cells, and (2) tubular blockage, the latter possibly resulting from the precipitation of myohæmoglobin casts in the tubules.

While no final conclusions can be stated regarding therapy, I think we may now approach the problem of treatment on a rational basis. Instead of waiting two or three days to find out whether or not kidney damage is manifest, we must think of the kidney from the outset. It should be impressed on rescue parties that the real danger in people with crushed limbs is that of renal failure. Before the patient is released, therefore, every effort should be made by means of abundant warm drinks to ensure a good urine flow. The advantage of a good diuresis may be: (1) the dilution of chemical poisons within the kidney tubules, and (2) the prevention of precipitation of myohæmoglobin casts.

It is important to realize that the kidneys are only damaged when the circulation is re-established through the crushed limb, i.e. after release. It would be advantageous, therefore, to apply a tourniquet to the proximal part of the limb before the weight is taken off, and this should be kept in position until the patient is in hospital. After this some control should be exercised on the restoration of circulation. The tourniquet may be replaced by a sphygmomanometer cuff which is deflated slowly below the systolic pressure. By this means a sudden flooding of the circulation with toxic products may be prevented. During this phase no attempt should be made to warm the limbs, and the injured limb should, in fact, be kept cold. Cooling with ice packs might have the effect of slowing the circulation and decreasing the rate of tissue autolysis.

Alkalinization of the urine seems to be advantageous, and it is certainly a rational procedure to give alkalies, as the alkali reserve of these patients is often markedly reduced. Sodium bicarbonate and sodium citrate should be given by mouth (30-60 gr., 2-3 hourly), from an early stage. Other diuretics may be tried, but there is little evidence as yet to favour any particular one. Mersalyl has been a failure more often than it has succeeded, and as this drug may be a tubular cell poison, it is safer to avoid it.

It will be impossible to maintain a good diuresis in the presence of circulatory collapse, and shock must therefore be treated by transfusion, usually of serum or plasma because of the frequent hæmoconcentration.

Professor J. Shaw Dunn, restricting his remarks to the renal pathology in cases of crush syndrome, agreed with Dr. Bywaters in finding in the cases which he had examined important damage of renal tubular epithelium in addition to the presence of brown casts in the lumina. The lesion could be described as an acute tubular nephritis, while its accompanying functional disturbances of anuria or oliguria, marked loss of concentrating power, and retention of urea could readily be paralleled in mercurial nephritis of man and in experimental tubular nephritis of animals. In the present cases the lesion showed the remarkable feature that it was restricted to the lower segments of the nephrons, viz. the ascending limbs of Henle's loop and second convoluted tubules, whereas almost all the many and varied substances which, in natural disease or experimentally caused tubular nephritis, affected the upper segment, or first convoluted tubule. Selective damage of the lower nephron segments appeared to have been little known in human disease, and few substances employed experimentally have had this effect. It might be significant, however, that two substances which occurred naturally in the human metabolism, namely uric acid and phosphoric acid, had been shown capable of this effect. The former injected intravenously in the rabbit had been shown to produce not only this renal lesion but also the effects of temporary oliguria, loss of concentrating power and rise of blood urea. It has been suggested that the special localization of effects of these agents is due to acidification of the renal filtrate in the tubular segments concerned, and it

seemed probable that the localization of lesion in the kidneys of crush syndrome was also contributed to by acidification of the filtrate in addition to the usual factor of concentration. The presence of the brown casts of myohæmoglobin in the tubules was at any rate confirmatory of the view that the renal change was caused by a positive factor derived from muscle and carried to the kidneys in the blood-stream, rather than to loss of something from the blood into the tissues. From observations on experimental tubular nephritis, Professor Shaw Dunn agreed with those speakers who had recommended the early administration of abundant fluids by the mouth, with alkalinization, as a possible means of forestalling or lessening the damage to the kidneys.

Mr. V. H. Riddell: I have only two observations to make: (1) If a large number of casualties is admitted to hospital it is very easy to miss the early crush syndrome unless the casualties are systematically examined. Such a patient often looks very well and for this reason may temporarily be passed over in favour of examining someone in a neighbouring bed who appears to be more dangerously ill. The only way to avoid this and other mistakes is to examine each patient in turn, however rapidly, from top to toe, and then, in the case of the crush syndrome the tell-tale wheals or simply a localized erythema of the skin will draw our attention to the lesion. The nurse in charge can then be warned as to what is likely to happen, the first urine can be saved and not thrown away and the investigations begun at the earliest moment.

(2) We all know that the crush syndrome is associated with impairment of renal function, but it is perhaps not so well known that other injuries, including operative shock, may also be associated with depression of the renal function. The impairment of renal function following injury varies from a temporary anuria of twenty-four hours' duration to a permanent and fatal variety.

Attention has been drawn to this oliguria or anuria in different ways. At two of the hospitals I visited for the Medical Research Council, ordinary rooms had been converted into resuscitation wards and special sluices rather than hand-basins fitted for dealing with the large number of urine bottles which it was supposed would be used. After admission of several batches of casualties the ward sister noticed that these utensils were only rarely asked for by air-raid casualties.

At another hospital a physician on the staff had been investigating cortin excretion in the urine of air-raid casualties and found difficulty in obtaining the necessary volume of fluid for his estimations. At St. George's we noticed that male patients who are normally fairly free in their use of the bottle did not call out for it in the same way as they do in the more convalescent wards.

Grant, of the Clinical Research Unit of Guy's, has also pointed out that if the first specimen of urine in the shocked patient is examined, it will often be found to contain red cells and albumin. I have confirmed this, and am at present investigating the first urine specimen passed after all big operations to see how consistent a finding this is.

Captain D. Magner, R.C.A.M.C.: The following case is of interest in that the muscle damage was not due to prolonged compression, but rather to sudden severe bruising suffered in a motor accident.

A British soldier, aged 26, was struck a heavy blow by a lorry. On admission there were signs of damage to the left side of trunk and left thigh, and multiple fractures of the pelvis. The blood-pressure was **100/60.**

On the next morning, as he had not voided, he was catheterized and the 8 oz. of urine were found to show traces of albumin and small numbers of red blood cells. The blood-pressure had fallen to **78/58.** He was given a transfusion of stored Group O blood. The patient's blood was Group B. No untoward effects were noted during the transfusion. His general condition improved, but he did not void. Daily catheterization yielded only small quantities of urine which never showed hæmoglobin or pigmented casts. The blood urea rose progressively to 328 mg.% on the day of death—seven days after the accident.

Autopsy revealed subcutaneous extravasation of blood in the left flank, and swelling of the left thigh, multiple fractures of the pelvis, and considerable retroperitoneal hæmorrhage in the pelvic tissues. There was also hæmorrhage beneath the sheath and into the fibres of the left iliopsoas muscle. This muscle, those of the posterior abdominal wall on the left side, and those of the left thigh, were moist and œdematous.

The kidneys appeared normal except for some cortical swelling. The rest of the autopsy was negative except for a patchy bronchopneumonia in lower lobes of both lungs.

Histological examination of the kidneys revealed no sign of antecedent renal disease. The glomeruli were normal. The renal tubules contained many eosinophilic granular casts. These were most numerous in the medulla but a few were seen in the second convoluted tubules in the cortex and in the tubules of the medullary rays. In the tubules containing casts there was some necrosis of epithelial cells and some evidence of epithelial regeneration. The interstitial tissue and blood-vessels were normal.

Comment.—It is true that the possibility of the case being one of ordinary transfusion reaction cannot be excluded as the man received a quantity of stored blood. However, the lack of lumbar pain or rigor at the time of the administration of the blood, and the lack of jaundice subsequently argue against this, as does the fact that Group "O" blood was given. The case, therefore, is believed to be one of crush syndrome.

Mr. W. H. Graham: The following case I encountered recently is of interest in association with the pathogenesis of renal damage in crushing injury.

A man, aged 18, was injured when the lorry in which he was riding came into collision with a concrete structure. He was extricated almost immediately and received in the casualty ward within thirty minutes of the accident. At that time he was found to be shocked (B.P. 80/50), cold, clammy, pulse 120, temperature 97° F. (fig. 6). There

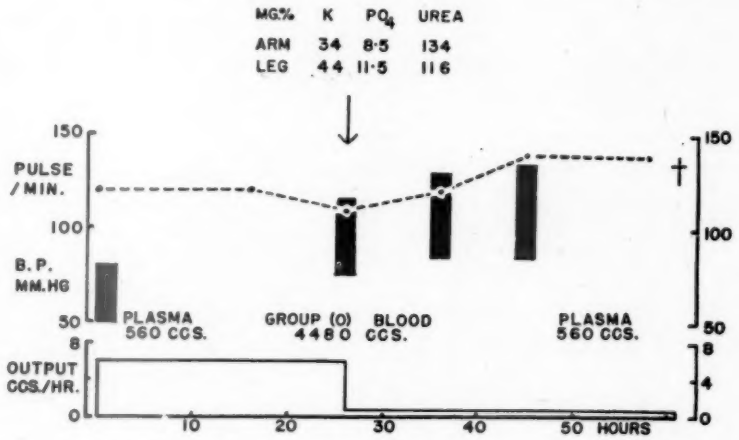


FIG. 6.—Chart showing course in Mr. Graham's case.
[KEY: Pulse—dotted line; blood-pressure—solid rectangle; intravenous fluid given; urinary output. Note oliguria.]

was a compound fracture of the right tibia and femur, and a simple fracture of the upper third of the left tibia in good position. Blood was issuing from the wound in the right thigh and from a deep laceration behind the left knee. Anti-tetanic and anti-gas-gangrene serum was given, the wounds were bandaged and splinted, and plasma (560 c.c.) and Group O blood (1,120 c.c.) given by intravenous drip. Sulphapyridine (2 g.) was given intravenously, followed by 1 g. intramuscularly every four hours.

Sixteen hours after admission the left leg was anæsthetic, cold, blue and pulseless, and the left thigh swollen and tense. Slight oozing only was seen from the wounds. 1,400 c.c. of Group O blood were given. The hæmoglobin was 51% (Haldane), pulse 120. At twenty-six hours, seen in conjunction with Dr. Bywaters, he was pallid, sweating and vomiting: B.P. 115/75, pulse 112. The left leg was warmer and of a better colour. Catheterization produced 150 c.c. of brown smoky urine which contained 60 mg.% albumin, 540 mg.% urea, and 85 mg.% NaCl, and gave a strongly positive benzidine reaction. A brown deposit formed, consisting of amorphous pigment granules: there were no casts, corpuscles or cells. Filtered urine gave a negative benzidine reaction. Venous blood samples were obtained at this time both from the arm and from the left foot (*see* Table I). The serum was not increased in colour.

TABLE I.—CHANGES IN BLOOD FROM ARM AND FROM BELOW LESION.

(*Bioch. Dept., British Postgraduate Medical School.*)

Venous blood : mg. per 100 c.c.	Arm	Foot
Urea	134	116
Plasma phosphate (as P)	8·5	11·5
Plasma chloride (as in NaCl)	512	489
Total plasma protein	6,500	6,500
Potassium	34	44
Hæmoglobin (% Haldane)	55·9	54·5

A further 1,400 c.c. of Group O blood were then given. Thirty-six hours after admission, he was of a good colour, dry and warm, B.P. 130/85, Hb. 56%, pulse 120. By forty-five hours he was alternately drowsy and restless, B.P. 135/85. The temperature had risen slightly to 99°, pulse 140. The thigh and leg were now less tense, he was drinking copiously, and vomiting a little. Further Group O blood (560 c.c.) and plasma (560 c.c.) were given. During that night he complained of pain in the loins; no urine was obtained on catheterization. His pulse became weaker and more rapid (140), temperature 101°, and he died sixty-one hours after admission. There was no terminal leakage from the leg wounds.

Post-mortem (seventy-two hours after death) by Dr. Skene Keith, showed slight œdema of the lungs and small petechiæ on the posterior surface of the heart. The kidneys were much swollen (the right kidney weighed 176 g.); the cortex was very pale and bulged considerably on section; the medulla showed many dark streaks. The left femoral vein and artery and hamstrings were completely severed at the top of the popliteal fossa, and a large fibrin clot was found here. The muscle above this level was normal. At the site, it was pale, and below of a somewhat rusty colour. That in the opposite leg appeared normal. The bladder contained 25 c.c. of brown urine giving a very strong benzidine reaction. There were many brown pigmented casts containing, rarely, cuboidal epithelial cell remains.

Microscopically, large pigmented casts were seen filling a large number of tubules. There were foci of œdema and cellular infiltration surrounding the ascending limb of Henle's tubule in the boundary zone, which, becoming necrotic, had liberated into the interstitial tissues hyaline casts. The muscle fibres from below the lesion showed patchy loss of staining ability and occasional vacuolation (*see* fig. 3). There was no inflammatory reaction and no arteriolar damage, but considerable œdema and, here and there, small hæmorrhages. Above the lesion the muscle appeared normal.

Comment.—Despite the resemblance to crushing injury, there was no prolonged pressure in this case, which appears, therefore, to fall into the group just mentioned by Dr. Bywaters, where muscle is injured by ischæmia, due, not to direct pressure, but to interference with blood supply.

[Thanks are due to the Chief Medical Officer of London County Council for permission to record this case.]

Mr. J. C. F. Lloyd Williamson and Dr. L. R. Janes: We have seen two cases recently where death from renal failure occurred following severe trauma to the limbs with compound fracture and vessel trauma.

CASE I.—A man, aged 24, was pinned for five minutes beneath an overturned Bren gun carrier. On admission one hour afterwards, he was found to be very shocked (fig. 7) and had compound fractures of the lower ends of both femora. After resuscitation, the wound was excised, and it was found that both the popliteal artery and vein were divided in each leg. Both limbs were packed with gauze and sulphanilamide powder, and enclosed in loose plaster. Next day there was some cyanosis of the feet, not improved by cutting the plaster, and some vomiting. Hæmoglobin was 100%. 2 oz. of urine obtained in the morning were clear, but 12 oz. later in the day were red-brown and contained casts but no red cells. On the third day he was restless, some sensation returned below the knees, and 16 oz. of clear urine were passed. Hb. 60%. On the fourth day, he passed 4 oz. of clear urine. Some mottling of the lower legs and feet, with red patches, was seen. On the fifth day, ½ oz. of urine was passed. He was not so well on the sixth day: urine (1 oz.) showed a faint trace of albumin and blood urea was 560 mg.%. He died in the early hours of the seventh day in coma, and was found to have 1 oz. of brown urine in the bladder. Post-mortem showed no jaundice: there was œdema of the legs, and a pallid necrosis of the lower end of the right vastus externus (5 cm. in diameter) was seen. The muscles of the legs and feet were œdematous

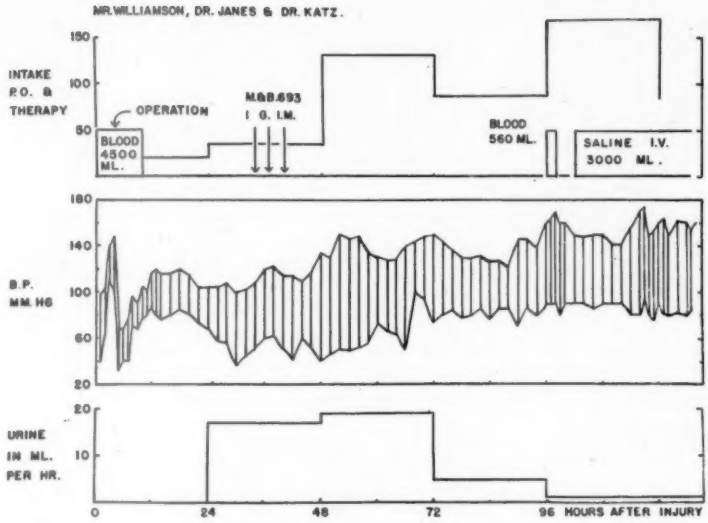


FIG. 7.—Chart showing course in Case I. Note increase of blood-pressure accompanying oliguria.

and viable though pale. There was dry gangrene of the right middle shin, plantar skin and terminal phalanx of the fifth toe, as well as of the skin and terminal phalanges of all the toes on the left side. The kidneys were swollen (7 oz. each) and stripped easily. The cortex was pale; the interlobular arteries were distended with blood. Microscopically the kidneys were similar to those seen in the crush syndrome.

CASE II (fig. 8).—This man was crushed momentarily between two cars, and on admission was found to be very shocked. There was a compound fracture of the left femoral shaft, and a simple fracture of the right pubic ramus. After resuscitation, a Steinmann pin was inserted through the tibia, and after excision of the wound, the limb was put up, with a loose plaster over the wound, on a Thomas' splint in extension. Next day he was conscious, and vomited 45 oz. The left leg and foot were white (except for petechial hæmorrhages and purple areas), insensitive to just above the knee and immobile. The muscles felt unduly hard. 8 oz. of thick brown-red urine were obtained by catheter (Table II). As there was no improvement, the limb was amputated at mid-thigh under gas and oxygen anæsthesia. Some of the muscle appeared to be greyish brick colour and non-contractile. The femoral artery at the upper end of the wound was pulsating, but, although intact throughout the lower part, it was inactive. Both it and the femoral vein were found to contain ante-mortem clot. Later that night a further urine specimen was obtained. Anti-gas serum was given. On the third day he was better; he vomited 8 oz. and excreted 8 oz. of urine, but by the fourth day his condition had deteriorated: the urine output was 4 oz., vomit 12 oz. The dosage of pot. citrate was maintained. Blood-urea was found to be 248 mg. per 100 c.c. He died on the morning of the fourth day, in coma, with a blood-urea of 288 mg. per 100 c.c. and a blood bilirubin within normal limits. Post-mortem, 6 oz. of urine were found in his bladder. There was no obvious sepsis or evidence of muscle necrosis. The femoral vessels were normal. The kidneys were swollen (12 oz. and 6 oz.) with some petechiæ in the pelves, and a pale swollen cortex. Microscopically, they resembled the kidney of crush syndrome.

Comment.—In such cases, if it is thought that renal damage is produced by absorption from the damaged limb, the practical question arises whether early amputation will be more effective: both cases presented evidence of muscle ischæmia, and in each there was a definite vascular lesion to account for it.

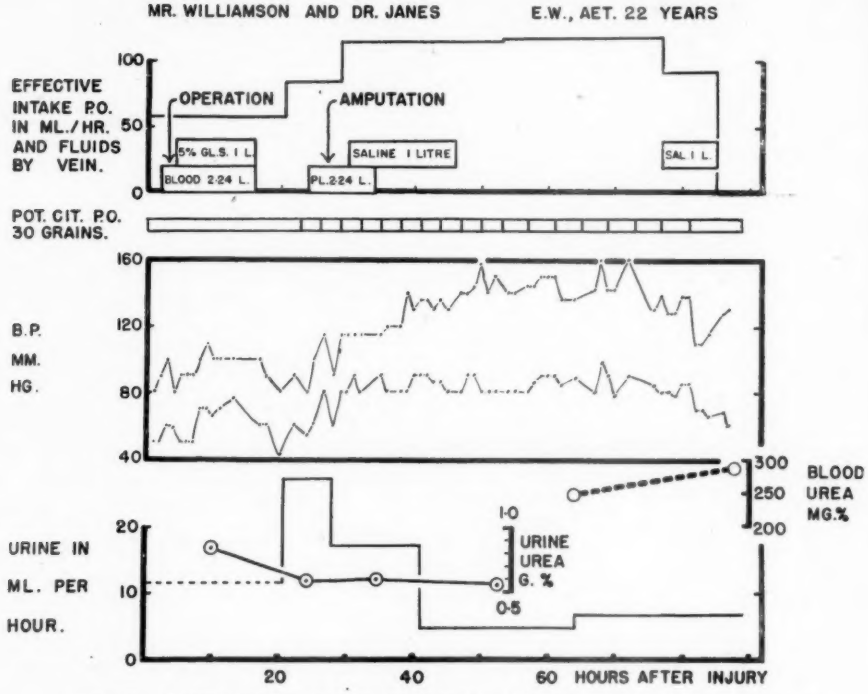


FIG. 8.—Chart showing course in Case II. Note increase of blood-pressure accompanying onset of oliguria together with poor urea concentration in the presence of raised blood urea indicating tubular impairment.

TABLE II.—URINE FINDINGS, CASE II (WILLIAMSON AND JANES).
(*Department of Biochemistry, British Postgraduate Medical School.*)

Time	Urea	Alb. mg./100 c.c.	Creatine g	pH	Supernatant fluid	Deposit	
						Colour	Micros.
2nd day 3.30 p.m.	830	200	0	4·7	Brown	Black	Pigment granules and epith. cells
2nd day 11 p.m.	590	160	0	5·3	Yellow	Dark brown	Pigment granules; no casts
3rd day 12.20 p.m.	590	180	0	5·5	Yellow	Dark brown	Pigment granules, red cells and leucocytes

Each deposit gave a positive benzidine reaction and showed the presence of acid hæmatin. The supernatant of the first specimen showed faint acid hæmatin bands. No hæmoglobin, methæmoglobin or myohæmoglobin bands were seen.

Mr. Ruscoe Clarke: There can be little doubt that minor degrees of renal disturbance following trauma, are frequently missed on account of their transitory nature. The following is a case of a major crush involving all the tissues of the leg resulting from an automobile accident. Shock and hæmorrhage necessitated the administration of blood and serum. The leg was amputated and a severe scalp wound explored. Recovery was uneventful. The renal changes were detected as a result of careful biochemical studies. Prior to operation marked oliguria accompanied a normal blood-pressure, This was presumably due to incipient shock. Its pre-renal origin is suggested by the

subsequent changes in renal function. During and immediately after the operation, a marked drop in blood-pressure was accompanied by polyuria while the urine at this time showed a high urea concentration, indicating normal renal function. Later on the rate of urinary output increased still further and numerous hyaline casts were present in several urine specimens. These we must assume had accumulated during the earlier phase of decreased renal function. After blood and serum transfusions amounting to a total of 5 pints the blood-pressure rose to normal and no further changes were observed. Combined clinical and biochemical studies in such cases will no doubt reveal many examples of such early changes in renal function.

Mr. Guy Blackburn: Sodium sulphate is undoubtedly of value in these cases. A good parallel could be drawn from its use in calculous anuria and after urological operations. Similarly both sodium chloride and sodium bicarbonate intravenously could be useful, the latter especially in raising the alkali reserve. This has been particularly evident in a case recently reported by me in the literature (*Brit. M. J.*, 1941 (ii), 475).

I feel that one should be quite clear as to the distinction between inability to pass water and suppression of urine in dealing with air-raid casualties; Munro's tidal drainage is a useful therapeutic measure with the first of these. Chemotherapy can be dangerous in crush injuries, where deposition of crystals in the tubules can easily enhance the degree of obstruction already present.

[*January* 7, 1942]

The Value of the Urinary Diastase in the Acute Abdomen

By E. B. C. Hughes, F.R.C.S.

SUMMARY

Some time before this war, an investigation was begun in an attempt to clear up the uncertainty surrounding this test. Some of the findings are reported here.

Lewison (1941) has presented results in some 700 cases of various abdominal diseases, and has summarized the literature. His conclusions give a very fair picture of the present beliefs concerning this test. He states in conclusion that: "Deviations from the normal (blood) amylase value occur infrequently in diseases other than pancreatitis. The range of these aberrations is restricted and unlikely to be a source of diagnostic error." Although the number of cases in this investigation is small, certain facts emerge which seem to contradict this statement, and to be of sufficient importance to justify their presentation.

The urine amylase has been estimated owing to the ease with which specimens could be obtained, and also in order to obtain some idea as to the value of a single urine estimation in the diagnosis of acute abdominal conditions.

The method used has been to incubate the urine with starch solution and to estimate the disappearance of the starch by means of iodine. Particular emphasis must be laid on keeping the temperature, pH value and quantities constant in each reading.

A large number of estimations were done, and amongst these were estimations on forty cases of acute peptic ulcer perforation. In these forty cases, four were found in which the urine diastase was over 300 units, and of a level previously thought diagnostic of pancreatitis. In addition three of these cases had areas of fat necrosis, and in these the pancreas seemed normal at operation. The fourth case had no fat necrosis present. At post-mortem the pancreas was found to be normal. In two of the cases the diastase level fell rapidly after operation to normal limits. In two the post-operative levels were not done. All were duodenal perforations in the anterior wall.

Three suggestions are made as to the possible cause of this finding. First, these cases may have had a separate area of pancreatitis. This seemed an unlikely combination, and neither the rapid return of the diastase to normal, nor the negative findings in the one post-mortem would seem to support this. Dr. Hamilton Patterson (1939), however,

informs me that he has performed a post-mortem on such a case. Secondly, these cases may have had other peptic ulcers on the posterior wall of the viscus, penetrating the pancreas and giving rise to a local area of pancreatitis. The previous history, the rapid return of the diastase to normal, and their uneventful progress does not seem to favour this possibility. Many such cases, however, have been described, particularly by Probstein, Wheeler and Gray (1939), and by Meyer and Amtman (1936). The third suggestion is, that at the time of perforation the viscus is filled with pancreatic juice and this is discharged from the duodenum, and hence adsorbed from the peritoneum.

It is believed that these facts are of some importance in view of the modern tendency to treat pancreatitis conservatively. It is possible that this diagnostic error may be avoided by estimating the diastase at higher levels, and preferably in the blood. A quick and reliable method has recently been described by Somogyi (1938) in which the estimation may be done in a few minutes without the necessity of incubating large numbers of tubes. This process is now on trial for these estimations in acute abdominal disease.

Estimations have been done on samples from many different hospitals and from many individual surgeons. I am, however, especially grateful to the staffs of University College Hospital, and of the Royal Sussex County Hospital for their help.

REFERENCES

HAMILTON PATTERSON, J. (1939), Personal Communication.
LEWISON, E. F. (1941), *Surg., Gynec. & Obst.*, **72**, 202.
MEYER, K., and AMTMAN, L. (1936), *Am. J. Surg.*, **33**, 307.
PROBSTEIN, WHEELER, and GRAY (1939), *J. Lab. & Clin. Med.*, **24**, 449.
SOMOGYI, M. (1938), *J. Biol. Chem.*, **125**, 399.

[*This investigation is still in progress. The amplified findings will be published later.*]

Tetanus in a London Sector in Two Years of War

By E. J. RADLEY SMITH, M.S.

AN effort was made to collect cases of tetanus occurring in Sector 9 by making them notifiable to the Group Officer. In the first two years of war seven, or possibly eight, such cases have been noted and some interesting features emerge from a study of their immunological and other characters.

CASE I.—Female, aged 50. Injured on 19.9.40 when the windows of her house in rural Surrey were blown in by blast while she was looking out. Her injuries were slight: cuts on the face and one hand. The cut hand became very mildly infected but when she was discharged from hospital on the ninth day all wounds were healed and she was quite well. 3,000 units anti-tetanic serum had been given at the first-aid post. She returned to hospital on the fourteenth day after injury complaining of stiffness of the jaw. There was great spasm of the masseters but apart from this the only other sign of tetanus which ever developed was that described by Gordon Holmes—the extension of the knee when the plantar response is elicited. She was successfully treated by 140,000 units of A.T.S. intramuscularly and by paraldehyde medication.

CASE II.—Male, aged 45. An air-raid casualty from South London, injured on 10.9.40. He was treated at the local hospital where 3,000 units A.T.S. were given on the day of injury. It is not known whether subsequent prophylactic doses were given at the two hospitals where he was subsequently treated. He had multiple severe injuries: laceration of left foot; perforating wound of left knee-joint; compound fractures of one metatarsal and phalanges of right foot and compound fracture of right radius. Gas gangrene developed in the right foot. His wounds were clean and healing well in December and his general condition was such that he was allowed home in plaster. On 6.1.41—three and a half months after the receipt of his injuries—he returned complaining of stiff jaws, back and neck. In a few days the condition had extended to clonic spasms of legs and abdomen and these continued up to 19.1.41. He was successfully treated with 660,000 units A.T.S. intravenously, intramuscularly and intrathecally and with sedatives.

CASE III.—A young soldier wounded in France a few days before his admission to hospital on 27.5.40 with a slight soft tissue gunshot wound of the lower part of the

back. The wound was evidently regarded as less severe than many others which were being admitted from Dunkirk and Belgium at that time, as it was not excised until the morning after admission, and he was not given a prophylactic dose of A.T.S. as supplies then available had been expended on apparently more serious cases. About seven days after the wound he developed severe tetanus, beginning with stiffness of the jaw, and died on the eleventh day after injury.

He received much A.T.S. (although the exact amount is not recorded) after the onset of the condition. Further, unlike the majority of soldiers, he had not been actively immunized against tetanus, possibly because he belonged to one of the first groups called up.

CASE IV.—Female, aged **55.** Injured in a bombed house at Abbey Wood on **7.9.40.** **3,000** units A.T.S. were given on that day at the local hospital. Her injuries were: A small wound of the neck opening the trachea; a small frontal scalp wound and perforations, which became infected, of both ear drums. On the fourteenth day severe generalized tetanus developed. She was successfully treated with **200,000** units A.T.S. and paraldehyde and avertin narcosis.

This patient's daughter, who was injured in the same house, had received a wound of the temporal region—a pebble had passed through the temporal muscle into the brain and later an intracranial abscess formed. The daughter also suffered from severe spasm of masseters and temporal muscles on both sides and may have been another case of tetanus, but I have not included her as the injury to the temporal muscle and the subsequent infection could have caused spasm.

CASE V.—Female, aged **39.** She was thrown out of her car near Dorking on **10.8.41,** sustaining a simple dislocation of an elbow; cut eyebrow; slight grazes on the knuckles and a wound of one popliteal fossa extending down to the muscles. The head and leg wounds were excised seven hours after their infliction and the latter was loosely sutured after the local application of sulphathiazole. **3,000** units A.T.S. were given at the time of the operation.

On the seventh day a serum rash developed and on the eighth at **9.0** p.m. she complained of shivering and stiffness of the back and shoulders which she had noticed for three hours. She was thereupon examined and found to have stiff jaws and brisk reflexes. At 9.30 p.m. a severe spasm of face, neck and upper spine occurred, and **20,000** units A.T.S. were given intravenously. At the end of this injection she collapsed and her blood-pressure readings were **65/50!** Throughout that night her systolic blood-pressure never rose above **80** and during the intervals of consciousness she complained that she could not see—possibly from cerebral anæmia. No further generalized spasms occurred but a risus sardonicus persisted throughout that night and the next day. Her treatment was most difficult because her general condition had been so profoundly affected by the, presumed, anaphylactic shock. Later rectal paraldehyde was given as her condition improved. She recovered after **120,000** units of A.T.S. had been given. She also received sulphathiazole orally as well as locally. The leg wound was never more than very mildly infected and the scalp wound healed by first intention.

The symptoms of tetanus appeared early—eighth day—and the generalized spasm was separated from the initial symptoms of stiffness by only three hours. Such a case with short incubation time and very short period of onset is usually fatal. She recovered after receiving what may be considered a moderate dose of A.T.S. for so severe a case. One wonders whether the severe anaphylactic shock might have had a beneficial effect. At one time, I am informed, severe specific fevers were treated by protein shock.

CASE VI.—Female, aged **45.** On **11.5.41** she was buried in the ruins of a bombed house where she lay pinned beside a hot stove. Her injuries were: Extensive superficial burns of one arm and thigh and extensive bruising without open wounds. She was given **2,000** (? 2,600) units A.T.S. on the day of injury at hospital. On the tenth day spasm of the jaw was noticed and despite large doses of A.T.S., avertin and sodium amytal narcosis she died on the twelfth day.

CASE VII.—Male, aged **45.** Injured by a bomb explosion in a Surrey town on **16.11.40.** His injuries were: Concussion with a scalp wound and a compound fracture of the fibula. **3,000** units of A.T.S. were given at the first-aid post but no surgical treatment was carried out for fifteen hours. The leg wound was clearly severely infected, for much secondary hæmorrhage took place, and his general condition was made worse by a lung infection and probable pulmonary infarct. On the twelfth day a stiff jaw was noticed and next day he died with arched back, locked jaws and spasms, despite much A.T.S.

Case	Type of tetanus	Physical injuries	Locality of receipt of injury	Presumed incubation period	Prophylactic dose of A.T.S.	Curative dose of A.T.S.	Active immunization	Result
I	Local	Clean cuts from glass	Chipstead, Surrey	14 days	3,000 u.	140,000	None	Recovered
II	Delayed	Compound fractures with gas gangrene	Peckham, S.E.	3½ months	3,000 u.	660,000	None	Recovered
III	Generalized and severe	Slight soft tissue wound of back	France	7 days (appr.)	Nil	Amount unknown	None	Died
IV	Generalized and severe	Small wound of scalp and trachea. Perforated drums	Abbey Wood, S.E.	14 days	3,000 u.	200,000	None	Recovered
V	Generalized and severe	Slight scalp wound and grazes. Simple dislocation. Mildly infected leg wound	Dorking, Surrey	8 days	3,000 u.	120,000	None	Recovered
VI	Generalized and severe	Extensive burns and bruises but no other wounds	Sydenham, S.E.	10 days	2,000 u. (? 2,600)	Amount unknown	None	Died
VII	Generalized and severe	Comp. fr. of fibula with severe infection	Purley, Surrey	13 days	3,000 u.	Amount unknown	None	Died

COMMENT

Only in Cases II, VII, and possibly V, where the injuries were severe, deep and involving muscle, did conditions arise which are usually considered favourable for the development of tetanus. In Case VI there were no wounds other than superficial burns, and in Case I only a few clean cuts caused by window glass which had all healed in less than nine days.

Seven, or possibly eight, cases have been recorded in Sector 9. All but one have occurred in civilian casualties and the only soldier who contracted tetanus had escaped the customary active immunization. Is this not significant? These cases have occurred in one Sector in *two* years of war. The figures for this Sector, available at the moment for only *one* year, show that 4,562 civilian air raid and about 6,500 Service casualties have been treated. Both civilian and Service casualties receive prophylactic A.T.S., but the troops have been actively immunized as well (Reg. Med. Serv. Army, 1938; appendix 10, para 6A) and amongst these so immunized no case of tetanus has been noted, although the most favourable circumstances for its development were surely to be found in the severely wounded from Dunkirk and Belgium who had often been virtually untreated for some days and of whom a considerable number did develop gas gangrene. Several Service casualties, other than battle casualties, e.g. motor-cycle accidents, injuries sustained on manœuvres with A.F.V., &c.—have contracted gas gangrene often in a severe form.

In all but one case prophylactic serum had been given soon after the wound had been inflicted. As far as is known this initial dose had not been repeated. E.M.S./Gen./246 not only advocates a single dose of prophylactic A.T.S., of 2,600 units, but actually explains why no further doses should be administered. Although this has been amended by E.M.S./Gen./333, which is still current and which advocates 3 doses each of 3,000 units at weekly intervals, it is to be feared that the earlier instruction still lingers in the mind since not one of the cases is known to have received a second prophylactic dose. Perhaps the type of wound did not suggest, in some of the cases, that tetanus was likely to develop,

and in all but one of them the three doses could not have been given as the incubation period was too short.

It is clear that one dose of 3,000 units A.T.S. given soon after the wound does not prevent tetanus. Further, it does not guarantee that should tetanus arise it will be local, delayed or mild, as is illustrated by Cases IV, V, VI, VII. This has already been pointed out by Cole (*Lancet*, 1940 (i), 167). In one case the tetanus was localized and in another long delayed, and this might be ascribed to the effect of the prophylactic dose. On the other hand Aldren Turner has recorded a case of chronic tetanus which had never received serum (*Proc. Roy. Soc. Med.*, 1939, **32**, 1413 (Sect. Neurol., 99)). Instructions are not likely to reach every doctor who may treat a casualty, and will not be remembered in detail, so that the optimum prophylactic treatment is almost certainly not applied in many cases.

The number of cases of tetanus here recorded is small, but they have been drawn from a large number of casualties, and it does appear that active immunization with tetanus toxoid, as practised by the R.A.M.C. is of great value. As this can be easily, and even advantageously, combined with anti-enteric inoculation (Maclean and Holt, *Lancet*, (ii), 581, and Ramon and Zoelter, *Ann. Inst. Pasteur*, 1927, **41**, 83), it would appear that the advantages of such active immunization should be laid before the public. The inquiries which the compilation of this brief report made necessary and other conversations with medical men have made it abundantly clear that many doctors still do not realize that every casualty, whatever the type or severity of wound, should receive a prophylactic dose of A.T.S. at once, and that this should be repeated on two further occasions. This state of affairs after more than two years of war may perhaps strengthen the case for active immunization.

The Immediate Replacement of Avulsed Soft Tissues

By P. H. Jayes, M.B., B.S.

A. C., aged 13, a gipsy boy, was bitten by a horse on December 15, 1941. He sustained a severe wound of the thigh as a result of being seized by the horse and tossed into the air. His mother, who witnessed the accident, discovered that a large piece of skin was missing from just above the knee. A few minutes later, she found the piece of flesh lying on the ground close to the horse. She picked it up, put it back on her son's leg, and bandaged the limb with boracic lint.

The accident occurred at about 12.30 p.m. and the boy was admitted to hospital the same afternoon at 3 o'clock. His general condition was good and soon after admission he was anæsthetized. It was found that a piece of skin and subcutaneous tissue had been completely severed from the lower part of the right thigh. The detached portion of skin and fat was lifted off the raw area and washed thoroughly in warm saline. Although it had contracted and at first seemed to be much too small, it actually represented the whole of the missing part. Except for one abrasion the skin appeared to be in perfect condition. It was pinned out on a board and all the subcutaneous fat was carefully dissected off its deep surface. In this way the avulsed tissue was converted into a full-thickness skin graft (Wolfe graft).

The wound measured about 7 by 3½ in. and extended down to the deep fascia. Its edges, which had retracted, were absolutely clean cut, as if with a scalpel. The quadriceps muscle was not damaged, but the upper half of the patella was exposed at the lower end of the wound.

The raw area was washed thoroughly with saline and hæmostasis obtained. Sulphanilamide powder was sprayed on to it and then the " graft " was applied. It fitted perfectly into the wound and it was sewn in position with fine silk sutures. A number of tiny slits were made in the " graft " with the point of a scalpel so as to provide an exit should any blood or serum collect beneath it.

Great attention was paid to the fixation of the " graft ". A roll of wool was soaked in flavine and paraffin emulsion and teased out into fine layers. These were applied to the " graft " and built up to form a thick, even pad. Gauze and wool were put on over this and a crepe bandage applied with firm pressure. The knee was immobilized by a plaster back-splint.

Convalescence was uneventful. The temperature rose to 99° F. on several occasions in the first few days, but the leg was comfortable and the dressings were not disturbed.

Sulphanilamide 1 grm. four-hourly was given by mouth for four days as a prophylactic measure. On the seventh day the bandage was removed and the upper and lower edges of the " graft " inspected. The appearance was satisfactory and the crepe bandage was reapplied without disturbing the dressings as a whole. On the tenth day all the dressings were removed. About 80% of the " graft " had taken well, the small area of loss being at the site of the original abrasion. This area is now clean and epithelializing rapidly from the edges. Healing should be complete in about six weeks from the date of injury.

Comment

In such cases, where the surgeon is presented with the avulsed soft tissues the possibility of immediate replacement should always be considered. The severed tissues must be treated in exactly the same way as any other graft. It would be futile to replace a piece of skin with a large quantity of fat attached; the fat should therefore be removed and the skin alone grafted back into place. The graft must be handled very gently and complete hæmostasis obtained before sewing it into position. Lastly, firm contact between the whole graft and its bed should be maintained during the period of healing.

Section of Ophthalmology

President—A. J. Ballantyne, M.D.

[*November* 14, 1941]

Angiomatosis Retinæ. Account of a Case, Including the Histological Results of X-ray Treatment

By Professor A. J. Ballantyne, M.D.

(*From the Tennent Institute of Ophthalmology, The University and Western Infirmary, Glasgow*)

This communication deals with a case of angiomatosis of the retina in which the large tortuous pathological vessels ended in an ophthalmoscopically invisible "capillary nævus" at or near the macula, no "massive exudate" having formed at the point of junction of the vessels. Fundus drawings show the appearances before and after X-ray treatment, and the histology of the retina and its vessels is shown in photomicrographs of sections obtained after excision of the eye, which was demanded on account of intra-ocular hæmorrhage followed by acute secondary glaucoma. The fundus appearance in this case closely resembled that of a case described by Mr. A. S. Philps at a meeting of this Section on February 10, 1939, and it was referred to in the discussion on Mr. Philps' case. My fundus drawings were reproduced in the *Proceedings*, 1938-39, **32**, 1261.

The patient, a young man, aged 19, was first seen by me at the Tennent Institute on December 4, 1936, having been referred by Dr. J. Pendleton White for an opinion regarding possible treatment.

Defective vision in the right eye was discovered after an attack of influenza about September 1936, and he had recently suffered from epistaxis.

Vision in the right eye: + 0·5 D sph./ + 2·5 D cyl. axis 90° = $\frac{6}{18}$; in the left eye: + 2 D cyl. axis 90° = $\frac{6}{12}$.

Ophthalmoscopic examination of the right eye (fig. 1) showed great enlargement and tortuosity of the lower temporal artery and vein, which met and formed a twisted loop

in the midst of an ill-defined, dusky, reddish-grey area as big as the disc and embracing the macula. The two large vessels were similar in colour and calibre, and could not be distinguished as artery and vein. The other retinal vessels were also somewhat dilated and tortuous, but arteries and veins were easily distinguished. The disc and neighbouring retina were œdematous and the disc of somewhat florid colour. There were no hæmorrhages or exudates. The left fundus was normal.

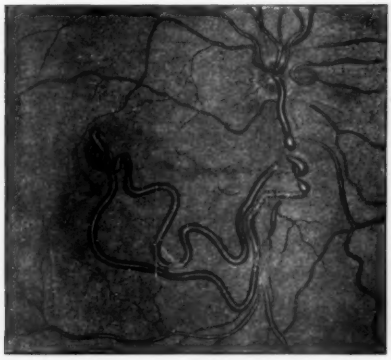


FIG. 1.

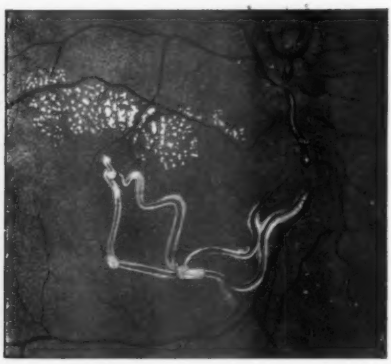


FIG. 2.

FIG. 1.—Angiomatosis retinæ. State of the right fundus before treatment. The pathological vessels are confined to the lower half of the retina.

FIG. 2.—State of the retinal vessels five months after X-ray treatment. The abnormal vessels in the lower half show thickening and opacity of their walls, and narrowing of the lumen.

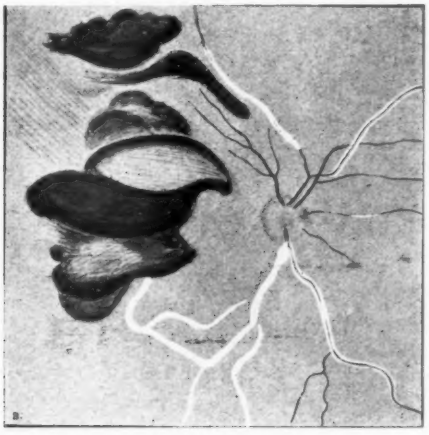


FIG. 3.—State of the fundus in the eye two years after X-ray treatment. (Binocular microscope × 7.) More extensive changes in the retinal vessels, especially in the lower half. Massive retinal hæmorrhages which had caused secondary glaucoma and led to excision.

A systematic general investigation was negative. There was not, nor has there ever been, any evidence of intracranial disease nor of hæmangiomata in any of the organs.

On the assumption that a hæmangioma was situated at the confluence of the two large vessels, four radon seeds giving a total of 4,000-5,000 r were placed on the sclera at the situation of the macula. A month later there was no change in the fundus picture, and radiograms showed that the seeds had not remained fixed in their original positions. He was dismissed, the vision of the right eye being $\frac{6}{36}$ (1 letter). Six weeks later he was readmitted, and X-ray treatment was begun on April 20, 1937.

The X-ray applications were made at three points: above the right eyebrow, near the outer canthus, and in the malar region, directed in each case towards the posterior pole of the eye. There were 14 treatments spread over three weeks and the total dose delivered at the treated zone was 4,750 r.

He was dismissed on May 8, 1937, with a fairly well-marked local reaction, which reached its peak, with redness of the lids and conjunctiva, corneal œdema and some turbidity of the aqueous, about six weeks after commencement of the X-ray treatment.

Eleven weeks after the beginning of the X-ray treatment the first ophthalmoscopic signs of a retinal reaction were seen in the shape of a white lateral sheathing of the central loop of the large vessels. Visual acuity in the right eye was now $\frac{6}{6}$. In about a fortnight a constellation of white spots, like those constituting a "macular star" appeared above the macula, and there was a progressive increase in the extent and width of the vessel sheathing, which throughout the whole period of observation of the fundus, was confined to the large abnormal vessels in the lower half of the fundus (fig. 2). The white spots varied from time to time; disappearing almost entirely for a period. At a later date patches of woolly-looking exudate appeared near the disc. Small patches of pigment on a pale background were also seen in the lower central area.

During the succeeding twelve months he suffered a good deal from recurrent neuralgic pain in and around the right eye, and this was relieved by alcohol injection of the trigeminus. Vision deteriorated and it became more difficult to obtain a good view of the fundus owing to œdema of the cornea, folding of Bowman's membrane, K.P., flare in the aqueous, and opacities in the lens. Other by-effects of the X-ray treatment were: loss of eyelashes, depigmentation of the skin of the lids, telangiectasis of the eyelids and conjunctiva bulbi, closure of the lachrymal puncta and a general rigidity of the eyelids.

On April 2, 1939, two years after the X-ray treatment, there was sudden loss of vision in the affected eye, due to a gross intra-ocular hæmorrhage, and the tension rose to 30 mm.Hg. This increased, and the eye became painful, with hyperæmia of the iris, as well as of the conjunctiva.

The eye was excised, and both the local anæsthetic injection and the removal of the eye were impeded by the very rigid state of the eyelids, the conjunctiva and the orbital tissues.

An artificial eye is now worn, but the shrinking of the skin and orbital tissues gives a sunken appearance to the right eye, and the inelastic condition persists.

There has been no pain during the last two years.

After fixation in formalin the eyeball was bisected in an equatorial direction, and the posterior half examined with the corneal microscope (fig. 3). The main inferior temporal vessels were seen to be represented by apparently solid white bands. One or two others of the inferior branches had a similar appearance while others showed a very narrow blood column heavily sheathed in white. The vessels in the upper half of the retina presented mainly a reduction and variability of calibre with a minor degree of sheathing.

To a large extent the central area of the fundus was occupied or covered by hæmorrhages of various types. Some of these were obviously in the anterior layers of the retina, some in the deeper layers, and others of more massive character either subhyaloid or under the internal limiting membrane. At two points there was a large oval mass of greyish colour with some resemblance to a cyst. This was afterwards found to be a collection of serum, separated from a massive hæmorrhage.

The two portions of the eye were embedded in celloidin and serial sections cut in an approximately vertical direction.

Interest naturally centred for the most part in the condition of the retina and of the retinal vessels; and especially in the nature of the reaction of the pathological vessels and the angioma to the X-ray application.

The histological picture was inevitably disturbed by the gross hæmorrhage, the more so as there was an interval of two months between the occurrence of the intra-ocular hæmorrhage and the excision of the eye. Moreover, for about a year before the excision

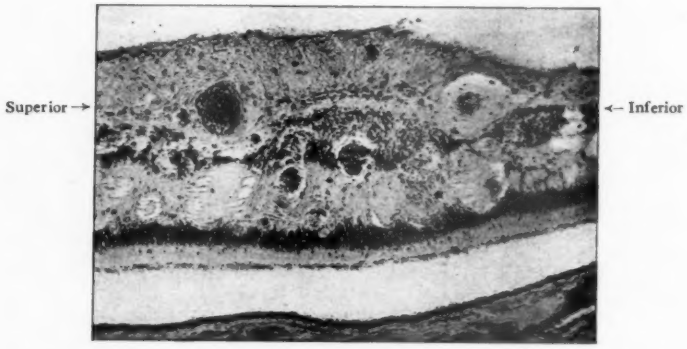


FIG. 4.—Section of retina adjacent to nasal disc margin. Shows contrast between inferior vessel with relatively thick hyaline wall and small lumen, and superior vessel with thick but less degenerate wall and relatively wide lumen. [Low power / Obj. 1″. Oc. 2.]

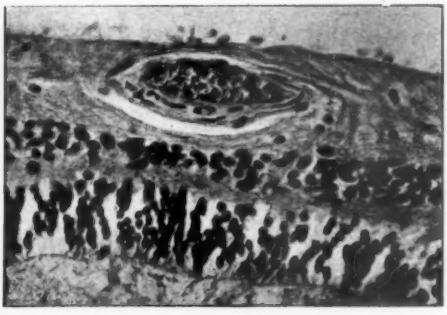


FIG. 5.—A vessel in the upper part of retina; hæmalum and eosin. The wall is thickened but the lumen is wide. [High power / Obj. ⅛″. Oc. 2.]

it was impossible to get a clear view of the fundus, on account of changes in the cornea and lens. But, at the same time, the picture seen in the excised eye by the corneal microscope, helped to bridge this gap, having a sufficiently close resemblance to the ophthalmoscopic drawing, made two years earlier, to enable us to correlate the clinical and the pathological changes.

Perhaps the most interesting and important clinical observation was the fact that the earliest changes seen with the ophthalmoscope occurred in the large pathological vessels;

and, indeed, so long as the fundus was visible there was no *apparent* change in the other retinal vessels. Twelve months later, however, inspection of the excised eye with the corneal microscope showed opacity in the walls of some of these, while sections revealed that there were practically no normal vessels in any part of the retina. The vascular changes, however, were notably more advanced in the lower region. Even the vessels on or near the disc show this contrast between those belonging to the lower and those belonging to the upper parts of the retina (fig. 4).

The clinical and pathological findings make it evident that the pathologically distended vessels were more radio-sensitive than the normal ones, and suggest that a smaller dose of the radiation, or similar doses spread over a longer period, might have produced the desired obliterative change in the big vessels without affecting the normal retinal circulation or producing the other harmful by-effects seen in this case.

One naturally hoped to find some histologically normal vessels and to be able to trace the sequence of changes from these to the completely obliterated vessels; but this was rendered difficult if not impossible by the radical differences between the vessels in the upper and lower halves of the retina above referred to.

It will be remembered that the accepted description of the vessel changes resulting from exposure to radium or X-rays (Colwell and Russ, 1934) is that there is a swelling of the collagenous elements in the vessel walls, proliferation and degeneration of the endothelial cells causing obliteration of the lumen, splitting of the elastic fibres and hyaline degeneration of the muscular coat.

If we examine some of the least abnormal vessels in the upper part of the retina (fig. 5), we find the walls thickened, and already showing a feebleness of the eosin staining, and a reduction in the number of nuclei. A single layer of endothelium is present, and the lumen of the vessels shows little, if any, distension or contraction. Only in a few instances can we find a thin layer of subendothelial tissue inside an internal elastic lamina. At this stage the Van Gieson and Mallory stains give the characteristic reactions of connective tissue; but Weigert's elastic tissue stain shows an increase of darkly staining elastic fibres throughout the whole thickness of the wall (fig. 6). Contrasting this with the vessels of similar size from the lower part of the fundus we find, in the latter, a similar weakness of the eosin staining, the zone nearest to the lumen being paler and poorer in nuclei, while there is a great reduction in the diameter of the lumen (fig. 7). Weigert's elastic tissue stain brings out the fact that the narrowing of the lumen is brought about by the presence of a thick, homogeneous feebly staining layer, within a coat composed of elastic tissue fibres similar to that described in the upper group of vessels (fig. 8).

It would appear then, that at this stage we see a notable swelling and degeneration of the collagenous elements of the outer coats of the vessels mingled with an abundance of elastic fibres, while in the pathologically distended vessels, associated with the angiomatous lesion, there is a greatly thickened intima, already reduced to a hyaline state.

The description already given applies to most of the vessels of the first group; but some of them show a reduction in the fibrillary character of the wall, and a feebler reaction to the Weigert stain, so that the wall throughout its thickness assumes a pale purplish colour and a structureless appearance (fig. 9). The lumen still remains comparatively open and there is no suggestion of the inner coat seen in the vessels of the second group. Among the latter, we can trace a sequence of more and more complete degenerative changes (fig. 10). The two coats remain distinguishable almost to the last stage, the outer one preserving a certain fibrillary structure, while the inner, sometimes separated from the outer by a sinuous refractile line, remains amorphous. Both become progressively paler, nuclear staining disappears from the outer coat, and the increasing thickness of the inner wall causes extreme narrowing of the lumen until we finally get a shrunken solid, hyaline, structure without a lumen and giving merely a pale purplish reaction to the Weigert stain.

There is little or no abnormality of the vessels in and around the optic nerve after it has left the eyeball.

I have made no attempt in this description to differentiate arteries from veins, as it seems to me impossible in these pathological vessels to do so with any certainty.

When the serial sections reach the macular region the retina is naturally greatly dis-

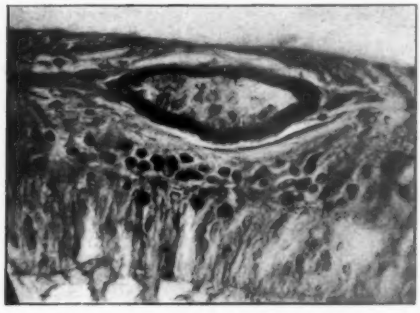


FIG. 6.—The same vessel: Weigert's elastic tissue stain. Proliferation of elastic tissue throughout the whole thickness of wall. No intimal thickening. [High power / Obj. ⅛". Oc. 2.]

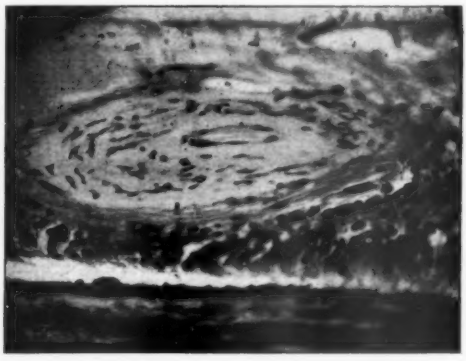


FIG. 7.—Vessel in lower half of retina; hæmalum and eosin. Great thickening of whole wall and very narrow lumen. [High power / Obj. ⅛". Oc. 2.]

FIG. 8.—The same vessel: Weigert's elastic tissue stain. The wall consists of two portions: an intima, greatly thickened and completely hyaline, and an adventitia composed largely of darkly stained elastic fibres. The lumen is very narrow. [High power / Obj. ⅛". Oc. 2.]

turbed by the bulky and extensive hæmorrhages and exudates; but we find here a compact mass of fibrous tissue covering an area about 2 mm. in diameter and occupying the nerve fibre and ganglion cell layers; with a maximum depth of about 0·5 mm. In this compact tissue, which stains to a brownish-red colour with hæmatoxylin and eosin, and which appears to be composed of glia, are found many irregularly shaped blood-filled spaces, as well as greatly distended capillaries and small vessels with more or less thickened walls. It seems fairly certain that this highly vascular area represents the angiomatous growth which forms the link between the large tortuous retinal vessels in the lower part of the fundus.

At a point in the lower half of the retina, a considerable distance below the macula, there is a small cluster of greatly distended capillaries in the nerve fibre layer. It is possible that this represents a small rudimentary angioma.

Throughout the greater part of the fundus included in the specimen, that is to say, over an area about 20 mm. in diameter, the retina presents a greater or lesser degree of disintegration. The changes are irregular in their distribution.

On the whole there is relatively good preservation of the retinal layers in the area below the disc and macula—the region of the pathological vessels. The upper half of the retina where the vessels were more normal, was the site of the first exudates (the constellation of white spots) and in the microscopic sections shows greater disturbance of the retinal layers.

FIG. 9.—The most advanced change in vessels of the upper half of the retina : a thick hyaline wall with a relatively large lumen. [High power / Obj. ⅛". Oc. 2.]

Œdema of the nerve fibre layer is widespread. Within and somewhat beyond the area disturbed by the hæmorrhage there are round or oval cavities in the inner molecular layer, in the inner nuclear layer and in the outer molecular layer. Those in the two inner layers are for the most part empty in the sections, but those in the outer molecular layer, which may break through into the inner and outer nuclear layers, are in many places filled with red blood corpuscles, albuminous exudate or masses of fibrin, a picture resembling that seen in so-called albuminuric retinitis (fig. 11). This type of lesion is most fully developed in the lower central part of the fundus, where the cavities in the outer molecular layer are very large and are separated from one another by stout columns of hyaline looking material (fig. 12). These spaces break through the inner nuclear layer into the inner molecular, and the nuclei belonging to the former are found scattered irregularly along the columns separating the cavities.

Exudates of albuminous character are found between the internal limiting membrane and the nerve fibre layer, or even extending deeply enough to impinge on the external

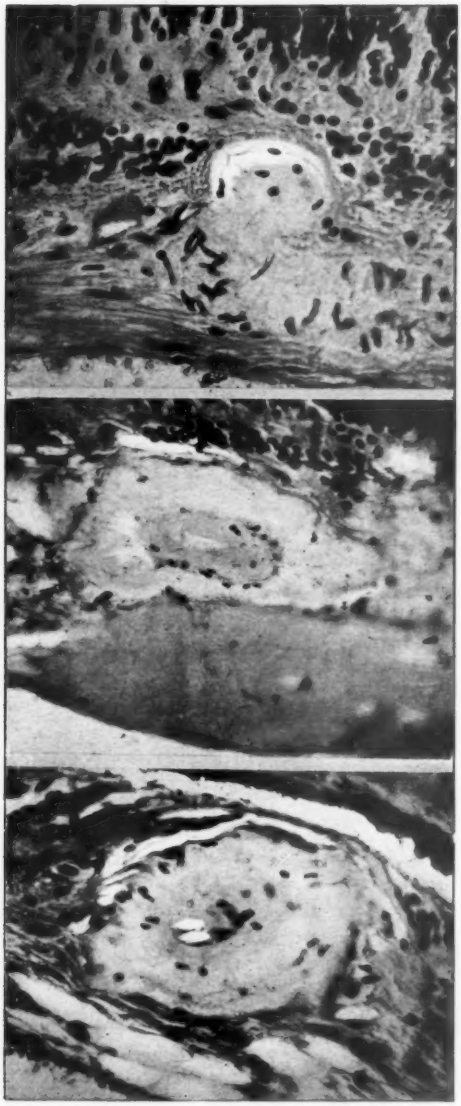


FIG. 10.—Three vessels, *a*, *b* and *c*, from lower half of retina, showing progressive changes. The adventitia, as well as the intima, becomes completely hyaline, the lumen diminishes and finally closes. [High power / Obj. $\frac{1}{6}$". Oc. 2.]

nuclear layer. Similar exudates are found between the rod and cone layer and the pigmented epithelium.

Hæmorrhages are a very prominent feature of the sections throughout the central area of the fundus, and they occur at all depths in the retina. Most prominent of all are those covering the macular region, which the microscope shows to be situated for the most part

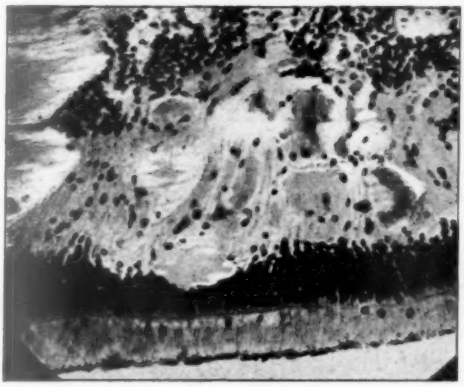


FIG. 11.—Disorganization of the retina, with formation of cavities in all layers, some containing masses of whole blood, serum or fibrin. The external nuclear layer is fairly well preserved but the internal nuclear is broken up and scattered. [Low power / Obj. 1″. Oc. 2.]

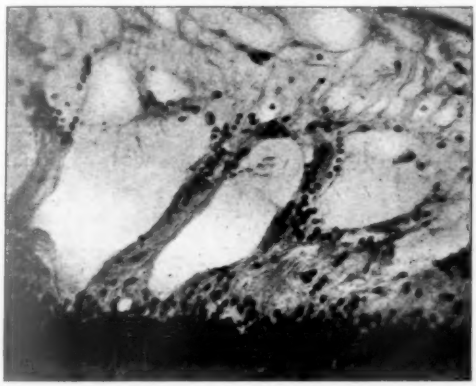


FIG. 12.—Large cavities occupying the external molecular, the internal nuclear and the internal molecular layers. [High power / Obj. ⅛″. Oc. 2.]

under the internal limiting membrane. In two situations coagulation has squeezed out a serum which lies in front of the massive hæmorrhage (fig. 13) and is represented in fig. 3 by the grey cystic-looking masses with a delicate striation apparently due to traction folds.

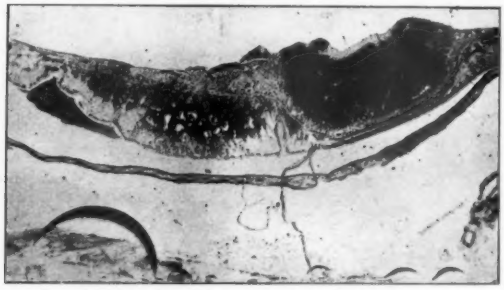


FIG. 13.—Section through the area of massive hæmorrhage, which also contains the angioma. Hæmorrhages are pre-retinal, intra-retinal and sub-retinal. The large dark hæmorrhage is within the angiomatous growth and lies entirely anterior to the inner molecular layer. [Low power / Obj. 1″. Oc. 2.]

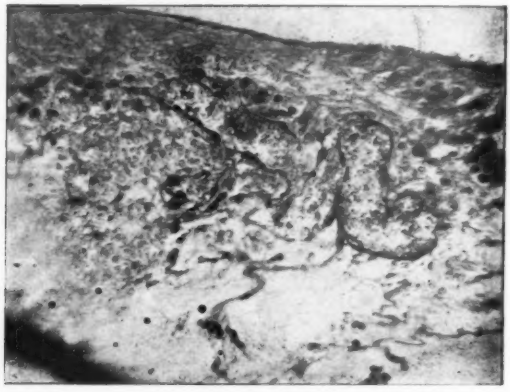


FIG. 14.—Dilated, thin-walled capillaries surrounded by retinal hæmorrhages [High power / Obj. ⅛″. Oc. 2.]

FIG. 15.—Site of the retinal angioma, which is situated within the nerve fibre and ganglion cell layers. Rupture of internal limiting membrane with escape of hæmorrhage into vitreous cavity. [Low power / Obj. 1″. Oc. 2.]

In addition to these intraretinal hæmorrhages there are hæmorrhages under the retina (between the rods and cones and the pigmented epithelium) as also in front of the internal limiting membrane. There was, of course, gross hæmorrhage into the vitreous, and a layer of blood corpuscles is found on the anterior surface of the retina in most of the sections. The least disturbed part of the retina is the external nuclear layer which, for the most part, presents a fairly normal and uniform depth throughout the sections. The rods and cones are well preserved in some places, destroyed in others. The ganglion cells in general are either scanty or entirely absent. The retinal pigment epithelium is intact in most of its extent.

It is difficult to judge the condition of the choroid in these formalin-fixed specimens, but it shows variations in thickness and apparently in vascularity from one point to another. In one area about the temporal limit of the large hæmorrhages, and some six millimetres below the macular level, the choroidal vessels have thickened hyaline walls, and over the same area (some 6 mm. in extent) the pigmented epithelium is of very irregular thickness, the retina is thin, with loss of its rods and cones and partial destruction of the other layers, and there is migration of pigment into the atrophic retina.

Far forward, behind the ora serrata, some sections show a collection of "ghost cells", mingled with pigmented cells (no doubt shed from the hexagonal pigment layer) lying between the rods and cones and the pigmented epithelium.

The optic nerve shows some atrophy of the nerve bundles and thickening of the fibrous septa. In the pial sheath there are many dilated blood-vessels, some with thickened walls.

In sections of the anterior segment of the eyeball, there are pathological changes in the cornea, iris and ciliary body. The corneal epithelium varies in depth and there is some desquamation of the superficial cells. At the limbus there is vascular pannus and round cell infiltration of the cornea and episclera. Over a small area in the lower part of the cornea there is destruction of Bowman's membrane. Descemet's membrane and the corneal endothelium are intact; but there are a few K.P. The ciliary body and processes show some atrophy. There is partial closure of the angle of the anterior chamber. In some of the iris vessels there is a thickened hyaline wall with narrowing of the lumen.

Comments

The occurrence of a capillary angioma of the retina in or near the macula is unusual if not unique. Junius (1930), describing a case in which the angioma was peripherally situated, but caused a central scotoma, remarked that up to that date no case of angioma at the macula had been reported: and I have failed to find any reference to such a case subsequent to the date of Junius' contribution.

It is unusual also for a case to come under observation before the angioma has become visible either as a red vascular nodule or as a pale globular tumour—an angiogliosis of the retina. It is noteworthy that in the present case, even after the vessels had reacted by showing thickening and loss of transparency of their walls there was no visible tumour mass at the macula.

Another case which was exceptional in this respect was that reported by Worms and Pinelli (1930) in which one of the large vessels returned to the papilla and the other seemed to sink into the retina, no angiomatous nodule being visible.

The difference in the reaction of the pathological and the normal vessels to the X-ray application is a point of interest and importance. While a few vessels in the upper half of the retina showed a very thin subendothelial internal coat, there is a very striking difference between this and the greatly thickened and degenerate intima seen in the vessels of the lower half; and it is difficult to believe that the first type of reaction was simply an earlier stage of the second. If we compare vessels from the upper and lower halves whose walls have reached the stage of complete hyaline degeneration we see that the first have still only one distinguishable coat, and an open lumen (figs. 5, 6, 9), while the second have two distinct coats and a more or less complete obliteration of the lumen (figs. 7, 8, 10). The latter condition seems to be that described as an endarteritis (or

endophlebitis) obliterans. The former does not fall into that category, and the sections do not show any transition stages between the one and the other.

The vessel changes in this case do not tally in all respects with those usually described as resulting from experimental exposure of healthy vessels to X-rays. Where cellular and nuclear staining is still present there is no evidence of proliferation of the endothelium. In the vessels of the lower retinal region the thickening which is causing narrowing and obliteration of the vessels is probably a proliferation of the subendothelial intima. Even in the capillaries of the angioma itself, there is no endothelial proliferation.

The demonstration of the histological explanation of the ophthalmoscopically "sheathed" vessels is of some interest. In a joint paper with Michaelson and Heggie (1938) it was shown that a white sheathed vessel, identified microscopically, presented atheromatous thickenings of the intima which had undergone a lipoid degeneration. It was pointed out that one would not be justified in assuming this to be the condition in every case of vessel sheathing, all that could be claimed was that the appearace of sheathing demanded the occurrence of a qualitative as well as a quantitative change in the vessel wall. In other words, a retinal vessel may be represented by a thread-like blood column although the vessel wall is ophthalmoscopically invisible, so long as the wall is thickened by mere increase of its normal structures. "Sheathing" only makes its appearance when these structures undergo hyaline, lipoid or some other form of degeneratino. In the present case there is no patchy thickening of the vessel wall, no eccentricity of the lumen, and no sign of a lipoid change. We find another kind of qualitative change, namely a hyaline degeneration of the whole vessel wall. It is interesting again to note that in many vessels of the upper part of the retina there was sheathing but no thickening of the intima, merely a hyaline degeneration of the thickened adventitia.

While it is possible, in microscopic sections, to identify the angioma at the macula, the extensive hæmorrhage makes it difficult to study this satisfactorily. No clear view of the fundus was obtained during the twelve months before excision of the eye, and, although the view of the fundus of the excised eye given by the corneal microscope was in a sense a substitute for ophthalmoscopic examination at that date, the hæmorrhage which had occurred two months earlier made it difficult to say to what extent the other retinal changes were due to the natural progress of the vascular lesion, the X-ray treatment or the damaging effects of the hæmorrhage.

The simple structure of the angioma serves to bring it into line with the view of E. T. Collins, v. Hippel, Leber and others that the primary lesion is derived from angioblastic sources, and is in fact a vascular tumour of congenital origin. The greater part of the tumour mass at this stage is composed of glia cells and fibres enclosing the wide capillaries and irregularly shaped blood-filled spaces, both lined with a single layer of endothelium. The gliosis would appear to be a secondary change due to local tissue reaction.

With regard to the source of the hæmorrhage, there is no direct association of the hæmorrhages with the larger vessels, indeed there is a comparative freedom from hæmorrhage in the lower part of the retina where these vessels are most abnormal.

Possibly the greater part of the hæmorrhage came originally from the angioma itself, and the neighbouring capillaries. There are many of these greatly distended capillaries buried among the hæmorrhages. Their walls seem to consist of a single layer of endothelium incomplete in some places as if from rupture (fig. 14). At one point in front of the angioma there is a rupture of the internal limiting membrane through which blood has escaped and is lying in a compact mass on the anterior surface of the retina (fig. 15).

In every case of hæmorrhage the attempt to explain its occurrence requires the consideration of three possible factors: the condition of the blood, the state of the vessel walls and the height of the blood-pressure. Most, if not all, of the hæmorrhages in this case are seen in similar forms in cases of hypertensive disease, with or without renal involvement; but it is very doubtful if the hypertension *per se* is an important factor. In the present case, there was neither hypertension nor any physical defect in the blood. It seems natural to attribute the hæmorrhage to the state of the blood-vessels. It is generally believed that the glial and connective tissue proliferation which produces the characteristic "massive exudate" in Coats' disease may be the result of sudden or gradual escape of blood from congenitally fragile vessels; and it is not improbable that in such

a case as this, a globular mass would have developed in the course of time in a similar way. Moreover, one of the early results of experimental radiation of vascular tissues is destruction of the endothelium of the vessels. And the integrity of the walls of the capillaries in this case would be further damaged by the anoxia resulting from impeded circulation in the partially obliterated vessels.

In the presence of hæmorrhages and exudative changes closely resembling those found in hypertensive retinitis it is surprising that there is almost complete absence of the so-called "ganglioform degeneration" of the nerve fibre layer.

I should like to express my thanks to Dr. J. Pendleton White for his courtesy in sending this case for investigation, and for giving permission for its publication.

REFERENCES

BALLANTYNE, A. J., MICHAELSON, I. C., and HEGGIE, J. F. (1938), *Tr. Ophth. Soc. U. Kingdom,* **58**, 255.

COLWELL, H. A., and RUSS, S. (1934), "X-ray and Radium Injuries". London.

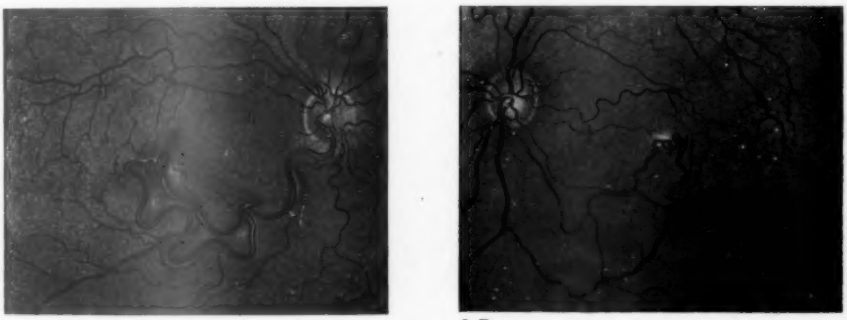
JUNIUS, P. (1930), *Arch. f. Augenh.,* **103**, 614.

PHILPS, A. S. (1939), *Proc. Roy. Soc. Med.,* **32**, 1260 (Sect. Ophth., 68).

WORMS, G., and PINELLI, J. (1930), *Bull. Soc. d'opht. de Paris,* **42**, 335.

Discussion.—Dr. BALLANTYNE in reply to the Chairman said that originally the tension was 30 mm. in the affected eye, but it went up after that. The tension digitally, as compared with the other eye was very high—probably in the region of 40 or 50.

Mr. A. SEYMOUR PHILPS showed two coloured drawings (fig. 1) of the eyes of a patient which had been shown at a meeting of the Section in 1939 (*Proceedings,* **32**, 1260). She was a woman of 35, with an arteriovenous communication in each eye. She complained very much of headaches and at a later stage of noises in the head. When the case was



R.E. L.E.

FIG 1.—Right and left fundi showing arteriovenous communication in each.

shown to the Section some members recommended diathermy, but others urged that it be left alone. The case was left alone, and the vision, which had been $\frac{6}{9}$ in each eye, became $\frac{6}{6}$. It was almost impossible to distinguish the arteries and veins except in so far as the branches of the vessels were not affected. In one eye the condition was not quite so marked as in the other at that time, but six months later she came back because vision in that eye had gone down suddenly; it was in fact $\frac{6}{60}$ and there was white exudate at the arteriovenous communication. No treatment was given, the patient was told to go home and rest. The vision improved to $\frac{6}{12}$ and there it remained, he believed, at the present time. The patient still complained of rhythmical noises in

the head, and had been twice admitted to hospital for a general neurological examination. The surgeon was now of opinion, however, that there was no general neurological lesion. The patient had listened so often to the descriptions of symptoms from which she should be suffering, that she had learnt them by heart.

Dr. BALLANTYNE said the point Mr. Philps raised about the vision having gone down owing to the presence of exudate, and the exudate disappearing, was rather interesting, and it would be useful to know what the precise reaction was, because nothing of the kind had been described so far. In most of the cases hitherto described and illustrated there had been a nodule at the confluence of the two big vessels, which no doubt began with the simple angioma. But what the explanation was of this transient change of the macula it was very difficult to say. Mr. Philps would of course follow up his case, and see what other changes took place.

In reply to Mr. R. H. Bickerton Dr. Ballantyne said that in his case there were quite clearly no similar changes in the other eye.

Section of the History of Medicine

President—J. F. Halls Dally, M.D.

[*December* 3, 1941]

Hospital Building—Past, Present and Future

By Charles E. Elcock, F.R.I.B.A.

(*Abridged*)

THE PAST

There appears to be reasonable evidence that in Ireland, Egypt and India, houses for the care and treatment of sick people were in existence 300 years before Christ. In Ireland they were called "Houses of Pity", but until the Christian era it would appear that sick people were considered somewhat burdensome and were indeed sometimes made away with if in the interest of the community. With the spread of Christian ideas in Europe it became usual for emperors and others to build and equip centres for the care of suffering humanity. Some of these were remarkable. The Basilias or Hospitium erected by St. Basil in Caesarea in A.D. 369 was a town of healing, separate streets being set aside for different groups of patients, with separate houses for physicians and nurses. In A.D. 400 Fabiola established houses for the sick in every quarter of Rome and there still remains a legend that she founded the existing hospital which bears her name in that city. When Augustine came to this country in A.D. 597 he founded a number of houses for the sick poor, called "bede homes" or "prayer homes", as it was thought that health was controlled by prayer. With the foundation of the great monastic orders in the fifth century and onwards, a cardinal principle was that of caring for the poor and infirm and ministering to their cure.

In A.D. 787 the Emperor Charlemagne commanded that every Bishop should institute a hospital, if possible near to the cathedral. This certainly initiated a development of houses for the special care of the infirm and poor. In England it is probable that A.D. 900 saw the establishment of the first English hospital by the then Archbishop of Canterbury. St. Bartholomew's Hospital in London was founded by Rahere, King Henry the First's jester, turned monk, about the year 1123.

The history of the Royal Hospital of Bethlem or Bethlehem is exceptionally interesting. The Charity was founded by Simon FitzMary in A.D. 1247. The first historical use of the hospital for "distracted persons" appears to be round about 1377. In 1346 the House was taken under the protection of the Mayor and Aldermen of the City of London. In 1403 the Priory of Bethlem had in it "six men who had lost their reason". In 1553 Bridewell Hospital was incorporated by letters patent. In 1676 the second hospital was erected in Moorfields, the architect being Robert Hooke, a genius comparable to Sir Christopher Wren, who was a colleague of Hooke. In 1812 the third Bethlem Hospital was begun in St. George's Fields, Southwark. The architect for this building was E. John Gandy in co-operation with the Hospital Surveyor—James Lewis. Many additions were afterwards made, the most notable being the dome and adjacent buildings which were the design of Sydney Smirke, and were carried out in 1844. In 1926 a magnificent country site of 330 acres was purchased at Shirley, near Croydon, and the fourth Bethlem Hospital was erected and opened in 1930. For this building I had the honour of acting as architect in close co-operation with the excellent surveyor to the hospital, the late Mr. J. A. Cheston. The development of the treatment of mental patients can scarcely be better shown than by a comparison of the plans of the 1676 building and those of 1812 and 1930.

THE PRESENT

Modern hospital planning may be said to have begun round about 1856—the Crimean War period—and was largely assisted by the wise and far-seeing counsel of Florence Nightingale. The Royal Bucks Infirmary at Aylesbury, Addenbrookes' Hospital at Cambridge, Winchester, Guildford, Woolwich, and a host of others were all products of this period, and were, for the most part, the outcome of voluntary and humanitarian ideals. This point requires stressing. It is one of those main historical trends referred to at the outset of this paper, a trend which is a direct development from the old religious foundations.

The passing of the Public Health Act of 1875 ushered in the principle that the health of the nation is the concern of the nation. This Act, with amending Acts—the Isolation Hospital Acts of 1893 and 1901 and others—led up to the Local Government Act of 1929, in which County Councils were required to make a Survey of all hospitals in their area and submit a report to the Ministry of Health. It further did away with the old Poor Law Guardians and required the establishment of Public Assistance Committees which had wide powers of co-operating with suitable voluntary and special hospitals in their areas and were empowered to build and equip further hospitals if found necessary and approved by the Ministry of Health. I was particularly interested in this development being appointed to make the survey and report for the Herts County Council. This Survey and Report was the first to be presented to the Ministry and formed a precedent for many which followed. The increased governmental interest in public health was reflected in the further development of the great and small voluntary hospitals throughout the country.

Within the last thirty years we have seen the development of methods of treatment scarcely apprehended in previous years. This required the hospital architect to devote much attention to a detailed examination of these methods so as to accommodate them with an understanding mind. Diagnostic and therapeutic X-ray departments, radium, sunlight, oxygen treatment, hydrotherapy and many other methods, with clinical, chemical, and pathological laboratories and enlarged out-patients departments and numerous other developments, have all placed the scientific planning of hospitals in the front rank of architectural achievement. The period mentioned has also seen the founding of specialized hospitals and a great development of facilities for the teaching of medical and surgical students. The development of hospitals and centres for treating varying types of mental disease was not remarkable for the introduction of new ideas in planning during the period under review. But during the last fifteen years great strides have been made, and the modern mental hospitals of this country are worthy of study and are thoroughly up to date.

It still remains an anomaly in our modern British life that the people who could afford to pay a reasonable sum for skilled hospital treatment have the least chance of that treatment and have either to be nursed at home or pay very high fees at private nursing homes. There is a need for a new type of hospital which, fully equipped and planned on modern lines, will serve the needs of what has been called the "white collar" patient. For some time before the war plans had been maturing for a large hospital of this type in London, in which it had been proved by skilled hospital accountants that the charge of £1 a day would cover all hospital costs, leaving the patient in the care of his usual medical adviser, the fees for professional services being paid by the patient as if at his own home. The completion of this project was postponed by the outbreak of war, but it is obviously a development which should not be lost sight of.

The establishment of therapy centres for the treatment of cancer throughout the country and the inclusion of mental treatment in general hospitals are two important trends in present-day hospital building. The maternity and child welfare clinics mark a very important advance in public health.

The actual planning of hospitals has developed from the ward as the central feature. At first large wards were the rule and persisted down to, say, ten or fifteen years ago. In the last fifteen years there has been a tendency to reduce the number of patients in a ward or to segregate them into wards divided by glazed screens, which allow for classification and a lessening of possibilities of cross-infection. In the planning of the extension of the Hertford County Hospital, it appeared to me that it was advisable to design an entirely new type of ward. The increasing appreciation of sunlight and air as valuable therapeutic agencies had made me realize that in our wards we actually used up

70% of the wall surface with bricks, the window openings forming only 30% of the whole. Surely the exact reverse should be the case? Again, the need for sunlight and air had led to the construction of wide and costly balconies which shaded the wards below and required the increased labour of wheeling beds in and out of the wards. Why not turn the wall space into long windows with suitably placed narrow constructional piers and by arranging these windows to slide open we could achieve at one operation the introduction of the maximum of sunlight and the benefits of veranda treatment? This developed the plan of what I have called the "veranda-ward" with the beds grouped between glazed screens, the beds being placed parallel to the wall instead of at right-angles. I have been glad to observe that this arrangement has been followed and copied in this country and all over the world. Australia, Japan, America, Sweden, Finland, and Italy all have examples of this veranda-ward, first introduced at the County Hospital at Hertford, England, in 1929. The plans and details were submitted to the Government Department of Building Research at Watford, who made two models—one of the old type of ward with beds at right-angles to the walls with window between the beds, and the other a model of the new "veranda-ward". These models were placed under an artificial sun which was placed at varying inclinations corresponding to winter, spring, summer and autumn. The Building Research Station prepared the following comparative table of the results which show that at all seasons the new ward gives more than twice as much possibility of sunshine as the old type of ward.

COMPARATIVE TABLE SHOWING VOLUME OF SUNSHINE RECEIVED BY OLD AND NEW (VERANDA-WARD) HOSPITAL WARDS.

	Direction of ward axis	Super-feet per day			
		Jan. 17	April 15	July 17	Oct. 16
Old ward type	N.-S.	1,236	2,517	2,089	1,830
	N.E.-S.W.	1,463	2,139	2,248	1,785
	N.W.-S.E.				
	E.-W.	1,776	1,480	1,494	1,841
New ward type	N.-S.	2,334	5,066	5,741	3,572
	N.E.-S.W.	2,873	4,264	4,522	3,524
	N.W.-S.E.				
	E.-W.	3,635	2,919	2,924	3,727

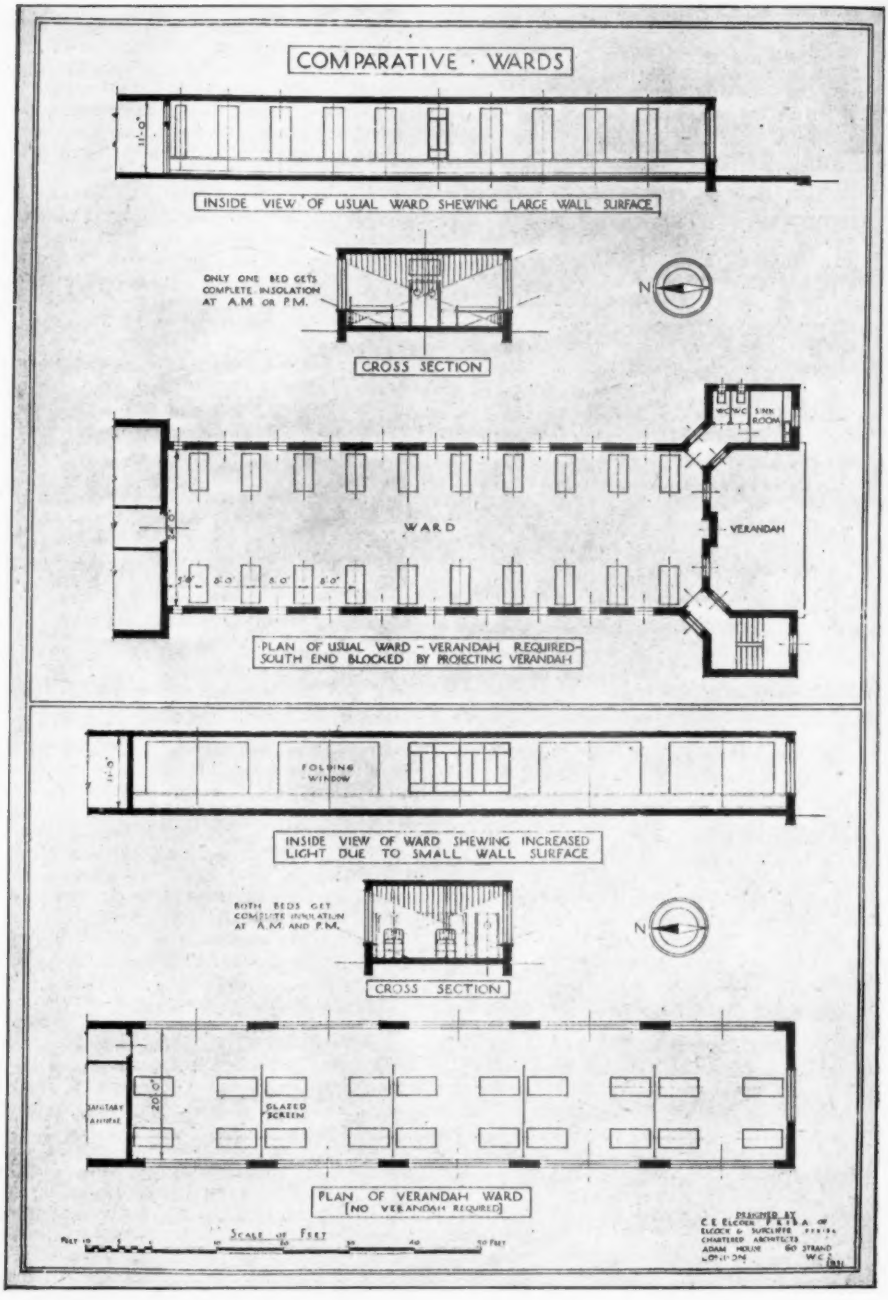
I have stressed this matter of the ward unit as it is in the interest of the patient. Similar developments are possible in almost every branch of hospital planning, which will lead to simplification, efficiency and economy in labour and cost. A great deal remains to be done in this matter of hospital planning, as from 1856 up to say 1914, hospital planning with few exceptions became standardized, crystallized and even fossilized. Complacency and tradition make bad masters. The stones they build with have time to gather the proverbial moss.

Sufficient attention has not been directed to the extraordinary variations in the cost of modern hospitals. The rough and ready method of assessing the cost at so much a bed has much to be said for it—provided the hospitals to be compared are of similar purpose and equipment. A large voluntary hospital lately erected in London at a cost of over £2,000 a bed is comparable to a somewhat similar hospital lately erected in the provinces at a cost of under £700 per bed. If allowance is made for certain special features in the London Hospital it is still impossible to agree to a figure of over £2,000 a bed. A Cottage Hospital in Wiltshire at under £500 a bed and fully equipped has to be compared with a similar Cottage Hospital in Yorkshire, erected at a cost of £1,000 a bed.

It is evident that there is an enormous divergence in the constructional cost of large hospitals of similar type. These variations include a lack of definite standards in the matter of accommodation, construction and equipment.

These essentials of modern hospital design should be agreed upon by a conference between medical men, the nursing faculty, hospital administrators and architects.

The architect must try and forget his little architectural tricks and details, and think more on the lines of a scientific "factory for health" rather than an imposing expanse of architectural display. The architectural effect will be gained by the dignity and sincerity of the planning and the arrangement of the masses without the expensive accretions of so-called architectural style, whether classic or modern. By the adoption of the


COMPARATIVE · WARDS
INSIDE VIEW OF USUAL WARD SHEWING LARGE WALL SURFACE
ONLY ONE BED GETS COMPLETE INSOLATION AT A.M OR P.M.
N
CROSS SECTION
WARD
VERANDAH
SUN ROOM
PLAN OF USUAL WARD - VERANDAH REQUIRED- SOUTH END BLOCKED BY PROJECTING VERANDAH
FOLDING WINDOW
INSIDE VIEW OF WARD SHEWING INCREASED LIGHT DUE TO SMALL WALL SURFACE
BOTH BEDS GET COMPLETE INSOLATION AT A.M. AND P.M.
N
CROSS SECTION
SANITARY ANNEXE
GLAZED SCREEN
PLAN OF VERANDAH WARD (NO VERANDAH REQUIRED)
SCALE OF FEET
DRAWN BY C.E. ELCOCK F.R.I.B.A. OF ELCOCK & SUTCLIFFE CHARTERED ARCHITECTS ADAM HOUSE 60 STRAND W.C.2

The Verandah Ward.

"health factory" type of plan, with its scientific clarity and flexibility of design, its elimination of all out-moded or unnecessary features, including unnecessary corridors, not only is capital outlay saved but large economies can be effected in annual administrative costs.

My "health factory" consists diagrammatically of a long hall 20 ft. wide placed with the axis east and west. Large folding windows on the south façade come between the supporting stanchions. A typical floor would be divided into units of 30 beds each, and might be three or six units long, and from three to ten floors high, depending on the number of beds required. In the centre of each unit on the northern side are placed the necessary subsidiary rooms, toilet rooms and utility services. Each unit is separated by a cross wall from the adjacent units, but communicates through the escape staircase lobby. Each utility wing on the north side has its own bed and passenger elevators and staircase, but there is no connecting corridor except on the ground floor. All internal walls can be removed without interference with the structure, which allows the utmost flexibility for future needs. All sanitary and main service pipes are in the northern service wings. The main structure would be of steel with thin external walls lined with non-conducting material and noiseproof floors, sanitary apparatus, piping and doors.

The economy of this system of planning is at once apparent when it is shown by this method that a complete General Hospital for 500 patients—without a medical school—fully equipped with all fixed fittings, without furniture but including the nurses' home and all the heating and electrical installation could be erected in this country in 1939 for under £600 a bed.

The elimination of noise is a matter to which considerable thought is being given, both noise from outside and the working noises of hospital administration. Much remains to be done in this direction, and it is obvious more town and city hospitals must remove from their noisy city centres to the more open spaces on the outskirts, with all sorts of consequent advantages. Much cheaper sites could naturally be obtained on the outskirts of large cities and the revenue derived from the sale of valuable sites in congested areas would greatly assist in meeting the cost of the new hospitals.

The Departmental Committee on the cost of hospitals set up in 1933 published its final Report in 1938 and extremely valuable data were registered. The war has prevented its consideration and implementation, but it must be followed up and its findings discussed by the people concerned or these valuable reports may be lost sight of.

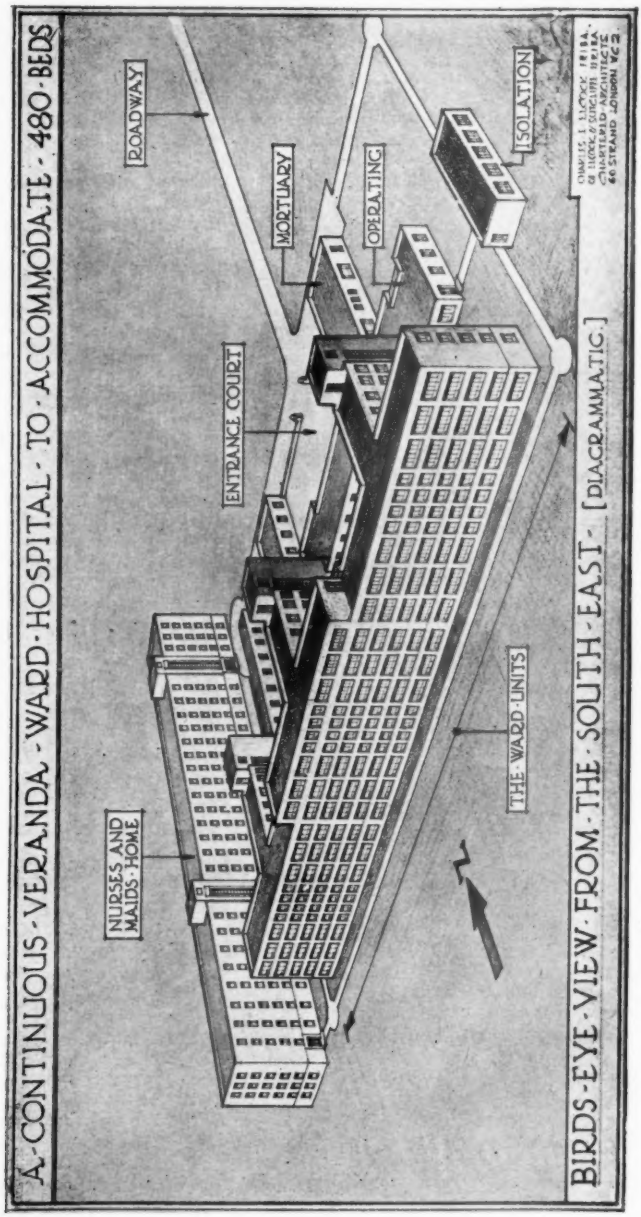
In the opinion of many the main thing which marks the present epoch in hospital history is the so-called "battle" between the voluntary hospital and the Government-controlled hospital. The present Minister of Health last October gave a lengthy exposition which was intended to clarify the position. The main thought underlying this appeared to be stated in the sentence: "It is accordingly proposed to lay on the major local authorities the duty of securing, in close co-operation with the voluntary agencies in the same field, the provision of such a service by placing on a more regular footing the partnership between the local authorities and voluntary hospitals." Whilst nothing definite appeared as to how this co-operation might be secured, it seems to dispose of the idea that this Government has any intention of attending the funeral of the voluntary system.

THE FUTURE

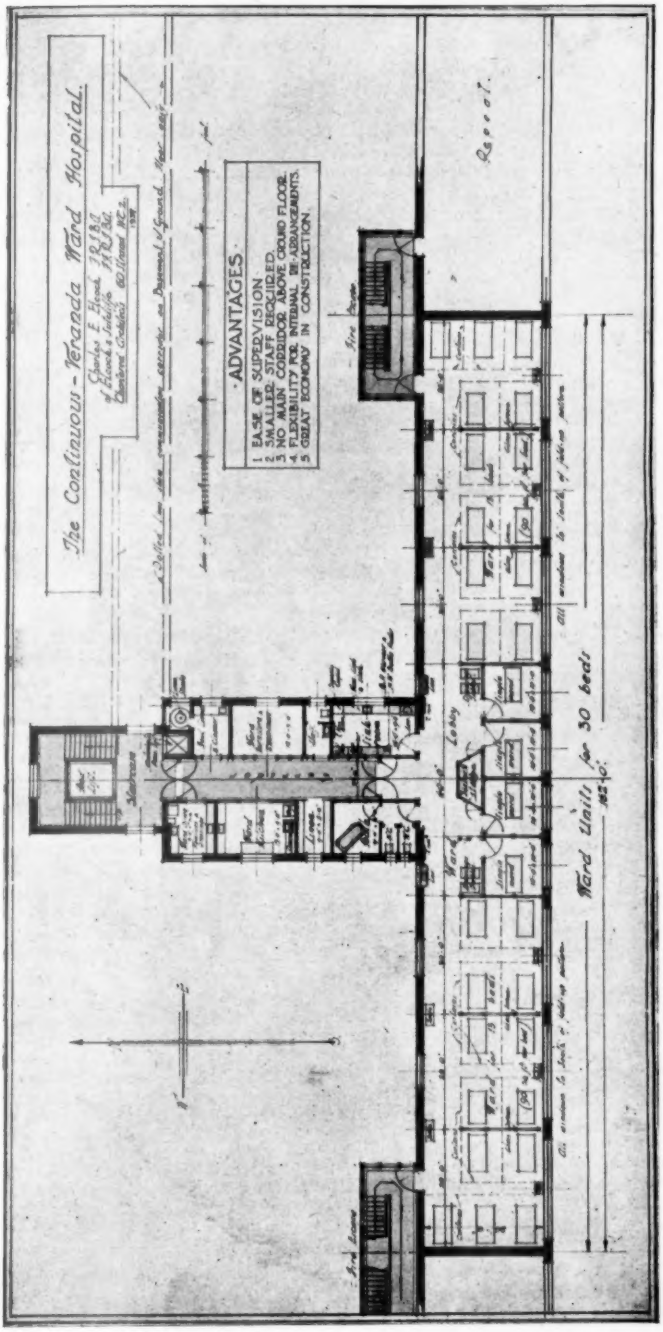
This pronouncement by the Minister of Health encourages conference, discussion, and co-operation, so that a *via media* to first-class organized hospital service may be discovered. If there is one thing democracy rightly watches with proper jealousy, it is the growth of bureaucracy.

Whilst, however, the growth of bureaucracy must be watched carefully, it should be open to free discussion entirely untrammelled by party politics as to whether it is really true that the health of the nation is the concern of the nation. Whether indeed a nation is of any use unless it is healthful. If these things are really true, a discussion would undoubtedly arise as to whether the health of the people should be a matter of private gain, or public expenditure. It may well be that conference might show that the enlargement of interest in healthful living as one of the first essentials of national well-being might actually bring about a great increase in public officials. If the whole thing had been authoritatively proved, such a bureaucracy would be an essential organ in a healthy national body.

This development might suggest the consideration as to whether an outside Board or



A "Health-Factory."


The Continuous - Veranda Ward Hospital.
ADVANTAGES.
1. EASE OF SUPERVISION
2. SMALLER STAFF REQUIRED.
3. NO MAIN CORRIDOR ABOVE GROUND FLOOR.
4. FLEXIBILITY FOR INTERNAL REARRANGEMENTS.
5. GREAT ECONOMY IN CONSTRUCTION.
Ward Units for 30 beds

Plan of "Health-Factory" Unit.

Corporation should not be set up by Royal Charter which should look after the nation's health, and should control all hospitals both governmental and voluntary. Through this Board or Corporation the expenditure of public money would be directly controlled. Money given by voluntary donation or subscription is just as sacred as Government Funds and it would be the sole aim of this Directive Health Board to see that the best use was made of finance, technique and science.

The Directive Health Board might have powers to examine critically all proposals for new buildings or extensions of existing buildings; it might have powers to veto work which did not appear to be in line with modern health proposals, it might have power to arrange areas or regions and obtain surveys of all health work in the areas and see what was redundant and what lacking. In the United States the College of Surgeons maintains a staff of inspectors, who visit each hospital, go over the medical and hospital records, and eventually issue lists of approved hospitals. If a hospital cannot get this approval its appeal for public funds is not certain of public support. All our hospitals should be subject to such examination, and it should be undertaken by this or some similar medical society.

This Directive Health Board would work under the Ministry of Health on somewhat similar lines to the Board of Control of Mental Hospitals, and would thus preserve a continuity of aim in harmony with national democratic methods of government. This whole question of national health and education for healthful living should be untouched by party politics and should be a matter for conference and earnest unbiased discussion—it might assist in ensuring the first essential of any nation—a people who know how to live healthfully.

But whatever is to be done must be attempted as soon as possible—there is no need to wait for the war to stop. Let conference begin, whatever may be the outcome there must be a stop to the amateur development of hospitals which have so frequently been dominated by the well-intentioned whims of the wealthy patrons. The advent of the great Rockefeller Trust of America with its skilled experts to guide its activities showed the way in which great wealth can competently assist in great health movements. The operations of the King Edward VII Hospital Fund and the formation of the Nuffield Provincial Hospitals Trust have already exerted and will continue to exert a profound and beneficial influence in hospital development, provided that those controlling the funds rely upon expert guidance to direct their activities.

And yet—even in the case of the magnificent Nuffield Trust, it might be pointed out that the activities of this Trust might possibly go further than assistance to voluntary hospitals and might with great benefit to the community thrust itself out along other less travelled roads and explore the tangled jungle of our social and industrial conditions. This trust is a great—a magnificent—thing, it may be thought ungenerous to even criticize its operations, but I am convinced the man who has donated to this country these munificent benefactions will be the first to agree that constructive criticism of this noble Trust will be welcomed.

I am emboldened as a layman to emphasize education in healthful living as the first essential of the future of hospital building, because I see this subject referred to so frequently by medical men of national and international reputation. Perhaps it is put very concisely by Dr. Wilinskey of Boston (U.S.A.) in an Address in 1939 where he said:

"I should like to emphasize the fact that the activities of hospitals in the field of public health keep apace and abreast of the newer knowledge of how disease may be prevented. Hospitals are carrying on many activities which are all-important factors in the control of disease and in the promotion of the public health. One who has a true knowledge of the complete functions of the hospital has an appreciation of the fact that one of the important functions is the constant teaching of people for more healthful living. If we are to prevent disease to its fullest extent, we must acquaint people with those facts which are factors in the reducing of illness to a minimum and in the promotion of health. The greater participation by the medical profession in the field of preventive medicine will call upon the additional resources of hospitals. In the administration of methods and techniques by which disease may be prevented, in the fostering of health habits, and in the carrying on of clinical activities for the conservation of health and the prevention of disease, hospitals, as in the past, will continue their onward march for the betterment of the human race."

Here we are in touch with something really big. On this high tableland we may feel the stimulus of a new and extended horizon.

What about the committees and medical staff of the future? I think most hospital architects will agree that they have sometimes to discuss the plans of large hospitals with boards and medical staffs and executives who are not well informed as to modern hospital developments. Very few have troubled to visit the United States or the fine new hospitals in Scandinavia or in other parts of Europe. How well-timed therefore was the public-spirited tour of these centres initiated and carried out by the Chairman of one of our newest London hospitals before the plans of the new buildings for the Westminster Hospital were finally settled.

The operations of the new health service will be frustrated if they are not directed by people who are themselves fascinated by the opportunity and thoroughly conversant with what is being done on similar lines in other countries. People who are incapable of being thrilled will be of little value in this crusade. For crusade it will be. All sorts of vested interests pledged to complacent acceptance of things as they are will be arrayed against this attempt towards national healthfulness.

The architects of the future will have more to do than plan hospitals, these committees and medical and administrative executives will be doing much more than working in and administering hospitals. For this wider vision of the people's health service is already here in our midst and has begun to operate, though in detached units.

The Pioneer Health Centre at Peckham was certainly a pioneer, an adventurer into unknown areas. The work of this health centre will in the future be known as a remarkable historic milestone in the endeavour to educate the public towards healthful living.

I venture the suggestion that this preventive work is actually of primary importance, the hospital being a secondary matter.

But there is a hospital in this country which seems to have struck a new note and is one of the signposts along the health road of the future. The new American Red Cross Harvard Field Hospital Unit in England is actually three services in one group. This Unit is to deal with epidemics, and consists of over twenty buildings. One of the primary services is the mobile field unit of public health doctors and nursing staff ready for service where required in any part of this country. The next service is the pathological and research laboratories, exceptionally well planned and equipped and staffed to undertake work coming to it from all over Great Britain. The third service is that of the very modern hospital for 125 beds fully staffed and now in active work. The whole of the buildings, equipment, heating, cooking, and laundry plant have all been shipped across from the United States, and have been erected ready for service in the course of five months. The whole of the medical, nursing and technical staffs are Americans who have—not without loss of life—risked the journey across here to establish this very modern hospital. Dr. John E. Gordon, the Director, is Professor of Epidemiology at Harvard University, and has been responsible for the arranging and planning. Speaking as a layman, I consider this hospital is one of the most noteworthy developments in hospital service in this country.

But the new movement does not stop here, and it is an active town in Lincolnshire which may possibly have the honour of being the first town in Great Britain to consider health service in the widest sense.

Early in 1939 the Board of this hospital were considering certain extensions and in order to place these correctly in relation to the present and future requirements it was necessary to make a survey of all the hospital buildings and site and plot them to scale and then review the future possibilities for, say, the next thirty years or so. With these plans before them it was asked if certain land should be acquired adjacent to the existing site. It thus became necessary to discuss what might be necessary in a post-war hospital. The Board have realized the development of preventive medicine and with a fine vision have not limited themselves to the mere provision of hospital accommodation, but have gone further. Having in mind the work of the Pioneer Health Centre at Peckham, and other similar ventures, they have now under consideration a scheme which will have education in healthful living as its main incentive. The scheme—which is in its preliminary stages—will certainly mean extension of the hospital, a new nurses' home, kitchens, out-patients' department, maternity unit, modern research laboratories and other hospital necessities, but it will also have as its main feature—preventive and educative therapy in the form of clinics, lecture halls and classrooms, swimming bath, outdoor and

indoor gymnasia, and a variety of other amenities all leading to the enthusiastic teaching of how to live healthfully, both for young and old.

To bring this most advanced project into being, many modifications will be necessary and it can only be attempted in stages.

I have endeavoured in the foregoing to indicate some of the main trends and influences of the Past on the Present of hospital building. Based upon these I have attempted the somewhat thankless task of suggestions for the Future. We must cease to think merely of hospitals as places to educate young doctors, instruct nurses, inoculate guinea-pigs or as elaborate plumbing depots—they must be part of the educational facilities of a community, where education in healthful living is actually the mainspring of their activities. I would suggest that the development of these health centres is something bigger than the provision of mere "health-factories"—health houses or hospitals. To me the wire fence round the cliff top is more interesting than the more spectacular ambulance at the bottom.

Personally, I am getting somewhat tired of the insistence on curing disease. I want there to be very little disease to cure. I visualize the abounding health and happiness of the people as becoming the greatest future glory of civic life.

It may appear a strange thing for an architect to say, but we can attach too much importance to buildings. It is what happens in the buildings that is the really important thing. It is not the great buildings of the Scandinavian countries which mainly arouse our interest—it is primarily the splendid, vigorous health of the people, the buildings being the outcome of necessity and not of mere display.

We have accustomed ourselves to point with pride to our huge medical centres and hospitals, quite forgetting that the greater these are, the greater is the shame that such things should be required. I can see a city with its parks, swimming baths, gymnasia, schools, community halls, hobby and craft rooms, with its museums and lecture halls, in which people can be taught how to eat and drink, how to dress, how to employ their leisure: in short, how to live rightly; and all these linked up closely and intimately with preventive health clinics of all sorts—infantile, adolescent and the adult, and round the corner, somewhat ashamed of its existence, the hospital, to take all those unfortunates whom accident or disease has laid low. Instead of health becoming associated with disease it will thus become associated with healthy living.

Going through the streets of our cities and small towns we see many people standing about at corners, lounging in bars, hump-shouldered and shabby, and in an ignorant effort to pass time away spending their money on "that which is not bread".

Educated and uneducated, we are people of few enthusiasms—not very vigorous in body or mind—nor do we want to be. After this war will come that satanic lassitude—the desire to sit still and let things take their course. This will be the real devil we will be up against. It will take all the enthusiasm we possess to combat this influence which will insinuate itself into tired minds ready for its opiate effect. These community health centres which I have endeavoured to outline would go far to engage the enthusiasm of young and old, would give opportunities to become acquainted with those vigorous and healthy activities of mind and body which would, in a generation, beneficially affect the individual men and women of the future.

This is the Health City of the Future. So we return to that conception of a City of Health which we saw in its initial form in Caesarea in A.D. 369.

Though up the steep paths of the mountain of experience stumbled our ancestors, as we are stumbling now—out of to-day's unparalleled sacrifice of life and treasure—the men and women of the future need not stumble, but at last come out on that fair straight road—whereon the wayfaring man, even though a poor fool, cannot err.

DISCUSSION

Dr. J. Ferguson (Surrey County Council): Mr. Elcock has put forward one conception which I think all of us who are engaged in public health will welcome, and that is the vision of the preventive side of hospital work, making the hospital a preventive centre. That is an idea which I am delighted to hear publicly ventilated.

The 1929 Act really marks a tremendous stage forward in hospital policy, and, therefore, in the hospital designing of this country. Broadly speaking, it brings the public authorities into the very forefront of the picture, and into the forefront of the Bodies responsible for providing hospital accommodation for the country. Since the war of 1914-18, owing to various causes—the changing social habits of the country, the living

FUTURE ROAD
NURSES HOME £179,180
NEW KITCHENS LAUNDRY DINING & MAIDS HOME £28,395
NEW HEALTH CENTRE
FUTURE ROAD
INCREASED WARD Nos £16,488
MATERNITY & ANTE NATAL £18,853
NEW OUT-PATIENTS DEPARTMENT & RADIO THERAPY £27,382
POOL
APPROX AREA 1 910 ACRES
APPROX AREA 1 910 ACRES
EXISTING BOUNDARY ROAD
CHILDREN
MANNINGTON ROAD
REFERENCE
COLOUR
EXISTING BUILDINGS TO REMAIN
NURSES HOME
MATERNITY & ANTE NATAL UNIT
INCREASED WARD ACCOMMODATION P.N.O. AND MATRON
NEW KITCHENS STORES DINING ROOMS LAUNDRY P.N. DN. & MAIDS HOME
NEW OUT PATIENTS RADIO THERAPY & TONSILLECTOMY WARDS
TOTAL ESTIMATED COST at JULY 1939 £91,290
DIAGRAMMATIC VIEW OF HOSPITAL SHEWING SHADOW DEVELOPMENT PLAN
BLOCK & ROGERS F.R.I.B.A. CHARTERED ARCHITECTS 48 BEDFORD SQUARE LONDON W.C.1.

in small houses, the shortage of domestic servants, and the increasing complexity of medicine, leading to the difficulty of investigating and treating cases properly at home, there has grown up in accentuated fashion what one might call the hospital habit. For all these reasons the municipal hospitals and the municipalities can no longer be content with providing accommodation for the physical derelicts of the nation; they must provide for the same types of medical and surgical cases as the voluntary hospitals. Therefore, unless you are to do the unthinkable thing of erecting hospital provision only for those who can afford to pay, the public authorities must in the future provide hospitals of the same standards of excellence as the voluntary hospitals. Therefore, one may expect to find a considerable and rapid development of new hospitals in the country as a whole.

I will say nothing about the Nuffield Trust; I will say nothing about the very much debated subject of Regionalization, except this, that large municipal authorities, like the London County Council, like Middlesex, and like Surrey, already have regional schemes in existence, with central purchasing, central direction of the patients to the appropriate hospitals, and so on. So much for policy.

One of the main contributions which Mr. Elcock has made to hospital design is the idea of the parallel bed. It is a very interesting idea indeed. It is an idea which was very fully explored by the Departmental Committee on Hospital Building Costs: but the conclusion which that Committee came to was that the evidence was not at that time great enough to come down whole-heartedly in favour of it to the exclusion of the projecting bed principle. The idea, however, is very attractive. I am going to pass round actual photographs of a hospital which the Surrey County Council has just built, an 860-bed hospital, which will be complete about April 1; and some of which is even now occupied. It is an interesting partial embodiment of Mr. Elcock's idea. A certain number of the beds, 12 in each ward unit of 30 beds, do face south, with beds which are parallel to the southern aspect of the hospital.

The more I see of the building of hospitals the more strongly convinced I am that it is vital to have specialist architects in order to obtain the best results. No doctor can in fact think of all the things which go to the making of a hospital. I urge, therefore, the most complete co-operation between the architect, the doctor and the matron, representing the nursing people, if the best results are to be obtained.

Mr. R. C. Harkness, F.R.C.S.: I would like to mention two aspects of importance. These are size and location. We have voluntary hospitals and municipal hospitals. The latter are a complex set of hospitals. Municipal general hospitals had their origin in the sick wards of workhouses and were at first almost entirely chronic hospitals, but now do much acute work. That has led in some cases to a dividing off of the chronic from the acute work. Other most important groups are the tuberculosis hospitals, which received their main impetus from National Insurance; and the fever hospitals, which were in existence somewhat earlier. The tuberculosis hospitals and the fever hospitals have been managed under public health powers. These sanctions coming at different times are largely responsible for these hospitals being in separate groups. Many consider that something should be done to link the various types of patients in one hospital. There are difficulties in getting the best medical staff, because of the narrow line of specialism and the slowness of promotion. It is sometimes held that medical staffs who treat special forms of disease can do their work better in close contact with those treating other forms of disease. If all these different forms of hospital work are to be brought together we must have large hospitals. Similar considerations arise in another way. Surgery, for example, can only be done to a proper standard if you have enough of it in one place.

The other important subject I want to refer to is the situation. Mr. Elcock has expressed the desire that hospitals should not be built in congested urban districts, but should be put on the outskirts. There are, however, other things which must be borne in mind, especially in big towns. Once when I was superintendent of a hospital I had an inquiry from the Ministry of Health asking: "I want you to explain why it is that your hospital admits x per thousand patients from the population you serve, whereas another hospital admits only half of x per thousand of its population." I replied: "My hospital is in the middle of the district which it serves." The other hospital was a more modern building on the outskirts but the patients tried to get into the hospitals nearer their homes.

Years ago a large voluntary hospital in a provincial town opened a new hospital on the outskirts. It was soon discovered that its patients were going to the voluntary hospital in a nearby municipality; subscriptions were going the same way. That is a thing which has to be remembered, I think. In war-time we can send patients where we like. When we get back to times of peace, I think we may find that it is not going to be so easy. There is a danger that we may build a hospital on the fringe of London and then find that it is impossible to use it for the purposes for which the original hospital was used, because the patients have drifted away.

Mr. W. E. Brooks, F.R.I.B.A. (London County Council): The L.C.C. has about 150 hospitals and institutions, apart from the numerous clinics, nursery and open-air schools under its charge. The hospitals are transferred buildings under the Act of 1929, and a similar survey was made in London to that which Mr. Elcock tells us he carried out in Hertfordshire.

This survey revealed that many of the buildings might well have been called "Houses of Pity"; but pity, I mean for the doctors, nurses and staffs who had to run them. The state of some of them was very unsatisfactory, but that did not apply to all, for numbers of them were, of course, first-class hospitals, and the bad ones are now very much better. Old wards in many cases have been turned about and divided up, as Mr. Elcock has shown, providing what he has termed "veranda-wards", with their consequent advantages.

Most of the hospital work at the L.C.C. has been in improving the transferred buildings; but many opportunities have arisen where new buildings were required, including new nurses' homes—which have been provided.

One point that interested me perhaps more than any other was in Mr. Elcock's reference to the health services and their effect on the national health, such as health centres, nursery schools, clinics, and other similar services.

We have built many of these smaller buildings: the medical room in the school, the clinics and nursery schools on the housing estates; camps and open-air schools for fresh-air treatment; all in consultation with the Council's medical advisers. In these we hope to teach mothers and children the elements of a healthy state of living. But we cannot stop there. Too many unhealthy and inconvenient houses still exist all over this land, and much of the good work done in the health centres is undone in the home itself.

When the war is finished, we may hope that this last and most important aspect will be tackled with all the energy that we can muster. I can speak with actual knowledge of the large amount that still remains to be done in London. The basis of good health lies in good, clean homes, with modern sanitation and cooking apparatus, together with the means of obtaining and understanding the use and preparation of proper food and suitable clothing.

"Buildings do not create a way of life—they only reflect it", and the work of the architect lies mainly in the interpretation of a developing social order in relation to the time in which he lives. He will provide the buildings, but it is for the doctors, nurses and teachers to educate the people to live in them.

Dr. W. A. Bullough (Essex County Council): I shall refer only to one important matter: the treatment of infectious conditions in general hospitals.

Research has thrown entirely new light on the way such infections should be treated. We have not implemented this knowledge in the design and construction of our hospitals. We have deliberately ignored the fact that persons may be admitted to hospitals in an infective condition or during the incubation period of such infective condition. This mainly concerns infants and children, who from time to time suffer from waves of measles, chicken-pox, whooping-cough, scarlet fever and the like. When these occur among children admitted to hospitals, we have dealt with the situation by various methods, including closing the wards and other stop-gap devices.

The additional expenditure in making the necessary provision will undoubtedly add to the cost of the buildings; but I am sure that in a short time, purely as a financial measure, it will be proved to be very sound. Apart from that, it is our duty to the patients to see that they are not exposed to avoidable infection.

We have in Essex an Epidemiological Committee which meets every month. The members have devoted a great deal of time to this subject, on which they have prepared a memorandum which has been sent to every hospital in Essex. The proposals are designed to prevent the introduction of infection into the wards; and in the case of failure, to control infections which have passed that barrier. They are briefly:

A reception room, with one or more cubicles and facilities for full examination, especially of the throat. The staff in that room would consist of a reception room medical officer, reliable and experienced, who would have full authority to deal with all admissions, under the supervision of the medical superintendent. He must, of course, have bacteriological facilities available.

Next, an observation ward, which should be cubicalized—the method of cubicalization depending on the materials available. Its size would depend on the size of the hospital. Here again, the medical officer would probably be the reception room medical officer, and would be responsible for the cases, which would be allocated to the appropriate physician or surgeon. The nursing staff in the observation ward must be experienced in barrier nursing and the nursing of infectious diseases. Full precautions would be observed re crockery, &c.

An infectious diseases ward and a septic ward, which again must be cubicalized,

would be provided. The size of this ward would again depend on the size of the hospital. It would have a small operating theatre attached to it.

All new admissions would be examined in the reception room by the reception room officer, who would admit to the infectious diseases ward any patient found to have any infectious condition, or any case in which diagnosis of infectious condition is in doubt. Any frank infectious condition would be transferred to the local isolation hospital. Thus the spread of infection would be limited owing to the fact that appropriate cases were either kept in the observation ward or passed on to the infectious diseases ward as required.

It is suggested that the number of beds in the observation and infectious diseases ward should be equivalent to 10% of the total beds of the hospital. In hutted hospitals a single hut might be divided, the two halves being used as an observation and infectious diseases ward respectively. In smaller hospitals side wards, or even cubicles, could be earmarked for these purposes.

These recommendations would have to be supplemented in many other ways to prevent the spread of infection—e.g. supervision over visitors, librarians.

With regard to the adult wards, it would be reasonable to cubicalize 15% of the beds, including the segregation of adults for other purposes. For the children's ward we suggest 30% of the beds should be cubicalized; this is rather a big figure, but from recent experience in Essex we think that nothing less can effectively control infection in general hospitals.

Dr. H. M. C. Macaulay (County Medical Officer of Health for Middlesex): There is one remark which Mr. Elcock made which should be underlined, namely, that the internal walls of his health factory should be capable of re-modelling without interfering with the main structure. It seems to me that the architect, as it were, crystallizes in a static form current ideas of medicine. But medicine is not static; it is vitally dynamic and the hospital which is up to date to-day, may be very far below our expectation in ten years' time.

Mr. Elcock's remark that the hospital of the future should be kept in as fluid and as elastic a shape as possible is one which should be endorsed. If our architect colleagues can give effect to that policy it may have a profound influence, not only on the structure of wards, but on out-patient departments and other buildings; and for years to come the hospital may be able to keep pace with the changes wrought by medical science.

With regard to prevention of disease it is a far easier thing to elicit sympathy for ministering to the care of the sick, than it is to enlist support for schemes of research and prevention. Curative medicine in its human aspect touches a very deep spring in human emotion, whereas the preventive side is a much more cold and calculating business. The cure of a single case of typhoid, by the exercise of medical skill and patient nursing may bring more gratitude than keeping a whole nation typhoid-free. It was with some such thoughts in mind that I listened to the remarks made by Mr. Elcock on the predominant part which, in his view, preventive medicine should take in any scheme in days to come. One is emboldened to hope that his view is shared by other enlightened laymen, and may in time come to be held by the public at large.

We medical officers of health who have had the administration and organization of hospitals placed upon us in recent years should perhaps realize that there is a danger of relegating to the background those preventive methods which are really the primary justification of our existence. Efforts have been made to link up the municipal hospital service with the preventive side of our work; but one of the difficulties with which we are faced is the fact that hospital medical officers are less interested in the preventive than in the curative side. Their training and experience lead them into the paths of the cure of disease. The training of medical students needs radical revision. It is still the usual practice in our medical schools for the whole field of preventive medicine to be covered by a series of perhaps a dozen lectures. Until social medicine is given the place it should have in the medical curriculum, we cannot expect to get the kind of preventive measures which the people of this country deserve.

Mr. C. D. Andrews, F.R.I.B.A.: Mr. Elcock referred to the "white collar" people and I would like to point out the treatment available for the "white collars" of Middlesex. These people have easy access to a most excellent municipal service at a graded fee according to income, the maximum being about £5 5s. per week. This is in hospitals costing £800 to £1,000 per bed.

The veranda-ward calls for a major discussion where many points of view could be expressed.

A previous speaker mentioned the necessity of the specialist architect; there is also the need for the specialist doctor, i.e. one who has studied planning extensively. This

need is reflected in a large number of hospitals which in first cost and in upkeep are unworthy of modern medicine.

Mr. Howard Robertson, F.R.I.B.A.: I was interested in what Dr. Bullough said about hospitals on the perimeter of towns. There is evidence, though this is perhaps a little away from Mr. Elcock's thesis, that there may be many towns, in which should be hospital centres.

One small point has relation to Mr. Elcock's allusion to the "Health Factory". As an architect, I would like to make a passing plea for the health hotel, as opposed to the health factory: because there is a great deal to be done through the form of architecture in the treatment of patients. I think there is a psychological effect of form and shape which we must develop. Perhaps when we have got through the factory phase, we may use architecture almost as a curative medium, quite apart from its functional purpose.

Mr. Duncan Fitzwilliams, F.R.C.S.: All hospitals need recreation rooms where patients can go and sit, read and play games. They should also have dining rooms. All military hospitals in the last war had this accommodation, but the lesson was lost when peace was declared.

The better to illustrate some curious features of hospital life, I am going to suppose that Mr. Elcock is ill and I am going to have him nursed in these pleasant wards which he has designed for the pleasure and comfort of the patient. It is his first night in hospital and he is in strange surroundings. There is a screen around the next bed and the nurses pass hurriedly to and from it. The Resident comes and whispers to the Sister. There is an air of gloom in the ward and the other inmates are strangely silent. Presently relations arrive and weep and Mr. Elcock realizes that some poor person is dying within four feet of his bed. Sights, horrible sounds, and even more unpleasant things assail his senses, and appal his strained imagination. Few people apart from the medical profession are familiar with death.

If there are any things which are private, birth is one and death is another. The dying person should have been removed to the privacy of a small ward where he can pass beyond the veil with his family around him without harrowing the feelings of twenty other people in a big ward.

All cases on the danger list should be removed from the big wards at once—they require quiet and many other things which can hardly be given without incommoding other patients. There should be no such things as "death wards", these are only the much-needed facilities for nursing the seriously sick. If they die, they do so decently; if they recover they return to the large ward, which should always be kept bright and cheery.

The next experience is just as repugnant. Mr. Elcock's meal has just been brought him; the kindly nurse coaxes him to eat, but is called away by his immediate neighbour who says something in her ear. A screen is put round the bed and a bedpan is surreptitiously introduced behind the screen. I will leave Mr. Elcock wishing him a good appetite.

Modern hospital beds have large wheels to enable them to be wheeled out on to the verandas, balconies and solariums, which are now considered the normal equipment of hospitals, and which Mr. Elcock has so well elaborated. Those same beds can be wheeled out, just as easily, to the lavatory accommodation which should be provided. In this lavatory these functions can be performed, enemas given and colostomies attended to.

Or again: Mr. Elcock has been admitted for some throat operation and, as he lies in bed, he sees a patient wheeled in from the theatre, still semi-conscious, vomiting and spitting blood into an ill-adjusted bowl which only receives part of what it is intended to contain. The whole spectacle is as disgusting as anything that can be imagined. On inquiry it is learned that it is "only a throat operation".

Recovery wards should be arranged close to the theatres where patients can be housed behind low cubicles so that the nurses passing down the centre can readily keep an eye upon them. Sexes do not matter in these circumstances as patients in this condition are sexless.

Suppose a head accident is admitted, restless, crying out and making such a din that no one can sleep. If the nurse leaves him she is called back by the other sleepless patients as the patient is attempting to get out of bed; or a patient suddenly becomes delirious from illness or alcohol; or a patient may become maniacal. There is little sleep for the sufferers in that ward that night; or possibly on many following nights. No London hospital has a ward where such noisy patients can be accommodated, though in Scotland they have long been considered a requisite part of the hospital.

It is the architects who must devise and carry out these reforms.

Mr. C. E. Kindersley, F.R.C.S.: I should like to emphasize one or two points that Mr. Elcock has brought out in his designs, the first being that as a primary principle a hospital is a building for a scientific purpose and should be designed to that end. Secondly, that the motto of hospital design should be: " that which has to be done most often should be done most easily "—a motto often ignored by architects. To illustrate this I can quote a ward kitchen placed, according to an architect's designs, and even approved by the Ministry of Health, 35 yards from the ward door and 52 yards from the furthest bed, and it took a lot of trouble on the part of the medical staff to have this defect remedied. I have seen a sterilizing room attached to a ward beautifully fitted, but with no space for the sterilizer where it could be provided with the necessary drainage and supplies, and wards designed with nowhere to put the essential basin. These are major crimes. Thirdly, Mr. Elcock mentions an all-important factor in hospital design which he has called " traffics ". The whole hospital design should be determined by traffics, and these traffics are not confined to the main corridors only; each department has its own traffics as well. Few appreciate that an operating theatre unit has at least five separate traffics in it—a point too seldom realized by those responsible for its design. A further suggestion he has made is that vertical traffics are better than horizontal traffics whenever possible.

Let a hospital architect attend to his design with the same detail that he would expect of a surgeon operating upon himself. The plea for health factories rather than hospitals should be considered, and conferences concerning hospital buildings and service should be called as soon as possible.

The Chairman: I think that Mr. Elcock has given us a sane, sober and constructive view of hospitals, and a wide vision for the future.

There are three points which struck me about his talk. The first is that the hospital should be a place of prevention. The late King Edward, speaking of tuberculosis, said: " If preventable why not prevented?"

With regard to historical events, Mr. Elcock referred to Rahere as being the reputed founder of St. Bartholomew's Hospital. St. Bartholomew's Hospital has been going since the year 1123. Rahere was prior of the Order of St. Bartholomew. His tomb is near by in the great Priory Church; and probably he had to do with the founding of the hospital.

I think that the hospital wards of the future should be built with sliding windows and veranda-wards and parallel beds.

When the Heart Hospital in Westmoreland Street, was designed, plans were drawn by a colleague of mine, Sir Sidney Russell Wells, afterwards Vice-Chancellor of the University of London, and myself. Those plans went out with the name of an architect on them because we did not want to put on our own names; but they were drawn exactly to our scale plans. We put the hospital kitchen on the roof because we had transport in mind and we also wanted to avoid the smell of cooking.

Post-war planning should begin now with conferences of those who are likely to be actively employed and interested in hospital building and post-war planning in general.

It would also be a useful thing for hospitals to be inspected at regular intervals because they vary a great deal in efficiency.

Mr. Elcock (in reply) stressed the urgent importance of conferences between medical men, the nursing and administrative services and architects, so that certain standards might be arrived at for future hospital and health services planning. This should lead to simple and direct planning with recognized suitable equipment, and economy in capital outlay and in annual administrative costs.

Section of Obstetrics and Gynæcology

President—J. M. Munro Kerr, LL.D., M.D., F.R.C.O.G.

[*January* 16, 1942]

Progress in Obstetrics and Gynæcology During the Present Century

PRESIDENT'S ADDRESS

By J. M. Munro Kerr, LL.D., M.D., F.R.C.O.G.

Though the title of my Address "Progress in Obstetrics and Gynæcology During the Present Century" may appear to be commonplace the subject itself certainly is not so.

THE PAST

At no period in its long history has obstetrics, and its sister branch gynæcology, made as great progress as during the present century. The leap forward, in which I and my contemporaries participated and which a younger generation is expediting, was not due to the efforts of obstetricians alone. It resulted in great measure from assistance we received, *first*, from scientists, (biologists, physiologists, biochemists, pathologists, bacteriologists) and, *secondly*, from the Public Health Service. I propose to develop later in my Address the theme that the closest possible co-operation by obstetricians, scientists and the Public Health Service should be the policy of the future, as only by this means will we ensure that progress in obstetrics and gynæcology does not lose momentum.

Let me briefly summarize the advances made during the first forty years of the present century. We speak of the *science* and *art* of obstetrics and gynæcology—let us take firstly progress in the science of our subject. At the beginning of the century we knew very little about "endocrines". To-day the profound influence their hormones exert on the growth, the nutrition, the mind, and even the character of the individual has in great part been revealed. Naturally obstetricians and gynæcologists are most interested in the influences exerted by the hormones of the gonads, of the pituitary gland, of the thyroid, and of the suprarenals, on the menstrual cycle; and the almost immediate activity aroused in them when an ovum is fertilized, as evidenced in the Aschheim-Zondek test. At the moment we can only speculate on the part they play in the growth of the uterus during pregnancy, in the activity of the uterus during labour, and in the involutionary processes of the puerperium. We have to admit, also, that application of our knowledge to practical problems has been disappointing. Hormonal therapy for functional disturbances of the reproductive system, apart from pregnancy, has not given the results hoped for. Possibly a little more encouraging are the results in certain dis-

turbances of pregnancy; but even here it cannot be claimed that much has been achieved so far.

Another great service, which scientists have rendered, is the proof they have furnished of the value of vitamins. Here practical application has followed close on the heels of laboratory findings.

Long before vitamins were discovered there was much discussion on the influence of diet on the size of the fœtus *in utero*—in these days the majority believed that the size of the fœtus in many instances, but to a varying degree, could be influenced by the food taken by the mother during pregnancy.

As I was desirous to obtain expert opinion *re* the possible injurious effect of excess of vitamins on (*a*) the individual in ordinary life, (*b*) the pregnant woman (more particularly as it might affect the size of her child), I wrote to Sir Edward Mellanby who passed on my letter to Dr. T. Moore (Director of the Dunn Nutritional Laboratory, Cambridge). Dr. Moore in his reply said:

(*a*) "As far as the first question is concerned, I think the risks are very slight. Even in experimental animals only vitamins A and D are known to be toxic when given in great excess.

"There is ample proof that excess of cod-liver oil is sometimes injurious to animals, although it is improbable that the toxicity is due to the vitamin content. In common with other marine oils, cod-liver oil seems to reinforce the effect of vitamin E deficiency in causing either muscular dystrophy or the interruption of gestation. . . .

"I myself would be against giving massive doses of cod-liver oil in pregnancy, and particularly so if the diet was low in vitamins B and E.

(*b*) "Excess of vitamins will not raise the rate of growth above normal, although deficiency may often reduce growth below normal.

"If an abnormal pelvis makes it imperative in expert opinion to attempt to limit the size of the fœtus by dietary methods, the reduction should be made only in the quantity of food consumed. Particular care should be taken to ensure that the vitamin content does not suffer as a result of the quantitative reduction."

This brings me to express my disappointment that more has not been accomplished to lessen the deaths from the "toxæmias of pregnancy". I cannot discover that we are much nearer a solution of the ætiology of *eclampsia* than when I attended Professor Leishman's lectures at Glasgow University over fifty years ago. In the latest edition (1941) of "William's Obstetrics", Stander, who has devoted great thought and much time to investigating the problem of eclampsia, is not prepared to do more than summarize the various theories which have been presented at different times. Possibly we see a little more clearly in respect to *hyperemesis gravidarum* which if caught early can almost always be arrested. Hypertension, persistent albuminuria, and the danger of chronic nephritis resulting therefrom, call for further investigation.

Radiography in obstetrics has made possible exactness of diagnosis, in respect of pelvic formation, position and attitude of fœtus, size of fœtus, plural pregnancy, malformations of fœtus, condition of the ureters and so on. In respect to minor pelvic abnormalities which are very common, great caution is necessary in determining for or against Cæsarian section from a pelvic radiograph. In the days preceding labour, and especially early in labour, there take place relaxation of the pelvic joints, little adjustments of the fœtal head to the pelvis and moulding of the fœtal head, which cannot be estimated before labour. Then again the strength of the forces cannot be predicted. Thus in many instances the most rational and scientific procedure is to allow a "trial of labour". Only by long clinical experience can the obstetrician learn to determine in particular cases whether a "trial of labour" is indicated or not, and to what extent the trial should be permitted to continue.

Radium and deep X-ray therapy has revolutionized the treatment of carcinoma of cervix and that troublesome condition of chronic subinvolution (chronic metritis?) of the uterus. Mention of carcinoma of cervix recalls to mind the perfection of technique developed by a number of operators in this and other countries when the radical (Wertheim) operation was the vogue. I have never been convinced that this wonderful operation should be discarded and entirely replaced by radium. It was very fortunate for the indifferent

operator when radium displaced hysterectomy, for the performance of a perfect Wertheim operation calls for very great technical skill.

Operative technique in both obstetrical and gynæcological surgery has made enormous strides in this century. When I was undergoing post-graduate training in Dublin, Berlin and elsewhere in the nineties—"the naughty nineties"—an aggressive *antiseptic* technique was employed. Many years passed before gloves and masks were introduced and an aseptic technique was perfected. The surgical technique of those days compared with that of to-day is as different as black from white. Consider the improvements in technique in such operations as the modern lower segment Cæsarian section, and the attention now paid to minute details in hysterectomy, myomectomy, salpingectomy, plastic operations for uterine and vaginal prolapse. Then again take the progress in the administration of anæsthetics which until recent years was considered by the family doctor to be his prerogative—to-day he does not desire to assume this responsibility. Specialists by perfecting anæsthetic technique in all its forms, have not only facilitated the surgeon's work, they have made possible operative procedures undreamt of early in the century. Very definitely, too, by careful choice of anæsthetic they have played an important part in bringing about the progressive lowering of the death-rate for all operations which this century has witnessed—here I would stress the great future for *block analgesia*.

I am convinced that the visits to clinics at home and abroad by both the Senior and the Junior "Visiting Gynæcological Society" have been of immense value to the members themselves, and to British obstetrics and gynæcology in general. The same can be said for our own special Journal. Under the direction of its Editor, Sir Comyns Berkeley, *The Journal of Obstetrics and Gynæcology of the British Empire* has been raised to a level equal to that of the best American and European journals in our speciality. The abstracts of current obstetrical and gynæcological literature, for which Frederick Roques is responsible, deserves special commendation. Furthermore, through our journal other countries have come to learn something of the great traditions and the cautious progress of British Obstetrics and Gynæcology.

But probably the greatest of all the corporate developments of the century, in our field of medicine, was the founding of the Royal College of Obstetricians and Gynæcologists. I wish to put it on record that this development of recent years was contemplated and discussed with me, when I was quite a youngster in obstetrics, by Sir Japp Sinclair, the founder of *The Journal of Obstetrics and Gynæcology*. But for all time the name of Blair Bell will be honoured as the founder of our College. His great benefactions and those of Lord Riddell to the College will ever be remembered with gratitude. Nor should be forgotten the services rendered by Fletcher Shaw, the indefatigable Secretary of the College during its years of protracted gestation and neonatal life, and now its President.

Another corporate development affecting our speciality is the Midwife Service which has been built up following the Midwives Acts of 1902, 1918 and 1926. I take this opportunity to extend to the Midwives Institute our congratulations on its new title—The College of Midwives.

To complete this summary of corporate advances I must mention once again the Public Health Service, whose serious invasion into our domain followed The Notification of Births (Extension) Act of 1915. As you are aware, by this and subsequent Acts, and especially by the Local Government Act of 1929, local authorities have been entrusted with the responsibility of ensuring that the maternity services of the country are satisfactory.

THE PRESENT

Putting aside such questions as the toxæmias of pregnancy, the treatment of functional diseases, and improvement in surgical technique already referred to, the problems which concern us more particularly at the moment are:

(1) The maternal death-rate and disability resulting from pregnancy and childbirth.
(2) The stillbirth and neonatal death-rate.
(3) Abortion.
(4) Birth control.
(5) Falling birth-rate.

(1) THE MATERNAL DEATH-RATE.—You are aware that the annual death-rate published by the Registrar-General includes deaths from: (*a*) Sepsis; (*b*) other diseases. It does not include (c) "Associated" deaths defined as "Deaths of women not classed to pregnancy and childbearing but returned as associated therewith". Let us consider the present position as regards each of these categories.

(*a*) *Sepsis*: It is cause for great satisfaction that there is an appreciable fall in the death-rate from sepsis in the last year or two. Here is the position for England and Wales.

Years	Death-rate per 1,000 live births
1925-30	1·7 (average)
1936	1·39
1937	0·98 (lowest on record)

How much further the death-rate from "sepsis" can be reduced is impossible to predict. The rate might in some years rise again should epidemics of infectious diseases develop, e.g. outbreaks of influenza; for epidemics of infectious diseases in the past have affected the death-rate from puerperal sepsis.

The pronounced lowering of the death-rate from sepsis is due to several factors, of which the following are the most important: (1) The drugs (sulphanilamides) now in our hands have furnished a weapon of inestimable value for combating infection should it develop. (2) A more thorough aseptic technique is being practised in the country generally. (3) Midwives who are responsible for so many deliveries in the country are a much better trained and more efficient body of women than ever before. Whether the fact that an increasing number of women are being treated in maternity hospitals may also be a factor cannot at the moment be determined. I, personally, am chary about making a statement on this point, because I am definitely in favour of institutional treatment as far as this is possible, and certainly for all primigravidæ.

(*b*) *Other diseases*: In this group improvement has been disappointing.

Years	Death-rate per 1,000 live births
1925-30	2·5 (average)
1936	2·41
1937	2·28

The toll of deaths from the toxæmias, hæmorrhages, and complications and accidents of labour (which include the bulk of the complications in this group) is much too high. All engaged or interested in obstetric practice are surprised and disappointed that in spite of the many antenatal clinics established by Local Authorities there is no marked improvement in the death-rate from eclampsia and other toxæmias in the country generally. I certainly had expected that by this time deaths from *eclampsia* might have been reduced by 20-30% at least. The reason is not far to seek. Antenatal care is still inadequate. The medical staffing of antenatal clinics under local authorities is in a great number of instances far from satisfactory. The individuals responsible for such clinics are out of touch with the practice of obstetrics as ultimately the patients are attended by midwives and/or other doctors—I shall refer later to remedial measures to correct this weakness in the antenatal services.

The deaths from hæmorrhages due to *placenta prævia*, and *accidental hæmorrhage* might well be lowered if the patient were immediately placed in an institution staffed by obstetric specialists on the first evidence of hæmorrhage or other untoward symptoms such as albuminuria, and heightened blood-pressure, which are so often the precursors of "accidental hæmorrhage". I need not remind you that in the interest of mother and child alike Cæsarian section is now accepted as the operation of choice for "placenta prævia", unless encountered in its simplest form.

Then take the deaths from *accidents and complications of childbirth*. Here again delivery in an institution by specialists would reduce enormously deaths from these causes. Some of the conditions responsible for these deaths can be recognized during pregnancy, e.g. pelvic disproportion; others, e.g. occipito-posterior positions of vertex may develop during labour. Many of the fœtal deaths are definitely due to faulty technique on the part of a doctor inexperienced in obstetric practice. There is room for improving purely obstetrical procedures such as manual correction of faulty position of

fœtus in pregnancy, vaginal manipulations in labour to bring the fœtal head into a more favourable position (which Smellie describes so graphically in his case records), gentleness in forceps delivery, breech extraction (associated with a very high fœtal mortality), and manual removal of placenta (frequently followed by shock and even death of the mother). Those and other little details of obstetric technique can only be learned by long apprenticeship and by constant practice.

(*c*) *Associated deaths*: In this group the death-rate has shown no improvement in recent years.

Years	Death-rate per 1,000 live births
1925-30	1·21 (average)
1936	1·10
1937	1·24

It is unlikely that there will ever be pronounced reduction in the death-rate in this group. Undoubtedly careful supervision of pregnancy and institutional treatment under experienced obstetricians and physicians would bring about a reduction in the deaths due to influenza, pulmonary tuberculosis, heart disease, chronic nephritis, &c., included in this group.

Maternal disability: There is no means by which we can compute with any degree of exactness the injuries, chronic infections of uterus and tubes, functional disabilities and ailments due to pregnancy and childbirth. We gynæcologists know, however, from the patients admitted to our wards or seen as out-patients, and from odd cases seen in consultation in the wards of surgical and medical colleagues, that a very considerable number of women are temporarily or permanently disabled.

McIntyre in an analysis of 7,734 patients treated in the Royal Samaritan Hospital, Glasgow, found that the ætiologic factor was:

Puerperal infection	...	...	...	28·1%
Trauma childbirth	...	...	...	35·3%

This unfortunate legacy from childbirth can only be reduced by more assiduous antenatal and intranatal care—the aphorism that "good obstetrics is preventive gynæcology" contains more truth than most aphorisms.

(2) Stillbirths and Neonatal Deaths.—During the present century the infant death-rate for England and Wales has fallen from 140 to 55 per 1,000 live and stillbirths; but the number of stillbirths and neonatal deaths has diminished only very slightly. Here is the position as presented in the last "Text" Volume of The Statistical Review of the Registrar-General of England and Wales (1937, Table XIV, p. 34).

Rates per 1,000 Live and Stillbirths.

Year	Stillbirths	Neonatal death-rate (ages 0-4 weeks)	Combined rate
1928	40·1	29·8	69·9
1929	40·0	31·5	71·5
1936	39·7	29·0	68·7
1937	39·0	28·6	67·6

We must set ourselves to lower the stillbirth and neonatal death-rates. The 8-10% of deaths due to malformations possibly cannot be lowered; but the fœtal deaths from prematurity and injury during birth can be reduced materially by improved antenatal and intranatal care, to which I have already made reference. I recommend a perusal of a recent article (*Lancet*, 1941 (ii), 657) on the subject, by Dugald Baird and John F. B. Wyper of Aberdeen; and the Commentary on it (*Lancet*, 1941 (ii), 746) by R. H. Titmuss, who promises a statistical study of the subject at an early date.

Here let me stress the importance of *research of clinical and practical problems* which are peculiarly the province of obstetricians and gynæcologists. The more intricate problems which can only be investigated in biological, chemical and biochemical laboratories have grown beyond the scope of the majority of practising obstetricians and gynæcologists. By all means encourage them to gain a practical knowledge of laboratory methods and carry out simpler laboratory investigations, but few young specialists can give time to

the long and arduous training this type of research entails—they will always remain amateurs. Possibly in the future—it has been suggested—there may be established in the country one or two large maternity units complete with clinical material (beds), and laboratories for every type of investigation. I wonder if it is feasible, or necessary, or advisable to attempt so ambitious a scheme!

(3) ABORTION.—There are a number of problems connected with abortion which are interesting obstetricians and gynæcologists at the present time. Take as examples—the influence of hormonal irregularity and vitamin E deficiency, the great loss of fœtal life, the progressive rise in criminal abortions and its influence on maternal mortality and morbidity, the legality of "therapeutic" abortion. Obviously I cannot do more than enumerate these problems, but I would like to express my convictions on three points: (*a*) That it is undesirable to press for "notification of abortion"; (*b*) that it is advisable to leave the Law governing abortion *in statu quo*. With the position as it is at present there is a freedom of action left us which we would never enjoy if the circumstances under which the performance of therapeutic abortion were defined by Act of Parliament; (*c*) Few if any of us are prepared to recommend extending the scope of the operation on economic or compassionate grounds as represented by the patient. There is still fresh in our minds the disastrous results following the free employment of induction of abortion in U.S.S.R. —results so disastrous that U.S.S.R. gave up the experiment.

(4) BIRTH CONTROL.—A dangerous development of the century is the extension of the practice of birth control. Not for a moment do I maintain that birth control is not justifiable by individuals in certain circumstances; but its free employment constitutes a danger to the country in which it is practised to anything but a moderate degree. That leads me to refer to the falling birth-rate.

(5) FALLING BIRTH-RATE.—Here is the position for England and Wales:

Years	Birth-rate per 1,000 of population
1881-90	32·4
1921-30	18·3
1939	14·9
1940	14·6

The danger for the nation is obvious. The Royal College of Obstetricians and Gynæcologists is alive to the danger. Eardley Holland represents the College on "The Population Investigation Committee". In the brochure entitled "Population and Fertility" issued by the Committee in 1939 under the Editorship of D. V. Glass and C. P. Blacker the following statements are made:

"The more closely the problem is studied, the clearer does it become that, in fact, the causes of the decline in fertility are numerous, complex and deep-seated. In Western European countries, they form so intimate a part of what we may call the twentieth-century view of life, that we can prophesy with some confidence that really effective counter measures will not be easy to find." (Page 6.)

"Surely what we should do to raise fertility is not to suppress birth control but to remove as many as possible of the obstacles which are impeding the free expression of the parental instinct. Conditions should be created in which people would *want* to have children and would have them deliberately and gladly. We should aim at minimizing, or if possible, removing the deterrents which now cause them, on balance, not to want children." (Page 99.)

There is little prospect that the birth-rate can be increased unless the Government is prepared to tackle the problem very seriously and introduce radical measures to combat the danger. Unfortunately no political party looks very far ahead or has much vision. That is left to small minorities who are designated "alarmists". Later, when the correctness of their views and warnings are confirmed, emergency measures are excitedly introduced and the minorities are then told that there must be no recriminations! I would warn the Government, as others have done, that the situation will become desperate in some years time—hurried legislation will then be too late!

Obstetricians can play a most important part in counteracting or lessening the grave national danger—*they must do everything possible to save fœtal life.* The number of fœtal deaths from prematurity, toxæmias, accidents and injuries in childbirth must (and can) be cut down; neonatal deaths must (and can) be cut down; the enormous wastage

of fœtal life from abortion must (and can) be reduced. This can only be accomplished by means of a National Maternity Service in which obstetricians and the Public Health Service (with all its ancillary agencies) are in full and sympathetic co-partnership. The sands are running out—no longer may we procrastinate and set up "Committees of Enquiry"—impending disaster is on our doorstep!

THE FUTURE

It can hardly be expected that advances in obstetrics and gynæcology in the second half of the century will equal in impressiveness those of the last forty years. There is reason to hope, however, that some of the problems I have referred to will have been solved, or at least be nearer solution, when the century closes.

It is probable that the efforts of obstetricians and gynæcologists in the immediate future will be concerned very especially with organizing the maternity services of the country.

Suppose I were to put the question: What is your ideal of maternity service? Would you not answer: To ensure safe conduct during pregnancy and childbirth for the expectant mother and her child. Then suppose I asked: Who are the most experienced in obstetric practice to carry out this work? Would you not answer: Obstetric specialists and highly trained midwives. Then suppose I went further and asked the question: Where can expectant mothers be best treated during labour, and if the need arise, for any complication in pregnancy, would your answer not be: A well-appointed maternity institution.

I agree that at the moment it is impossible to provide institutional treatment for all; but it is feasible and is being approached in a number of cities at home and abroad. It might require something in the region of 25,000 to 30,000 beds for England and Wales—that is only a very approximate estimate. The figure can easily be worked out and the cost estimated. Certainly domiciliary midwifery gives fairly good results; but most doctors do not have their wives delivered in their own homes; and they also advise their patients to be confined in an institution. Why then should not the wife of the artisan living often in very unfavourable surroundings in an industrialized city, or the wife of the black-coated clerk living in a tiny bungalow, have equally good treatment by experts and in equally good surroundings.

It may be argued that this means taking away the obstetric practice from general practitioners. No one holds general, or as I prefer to call them, family practitioners in higher regard than I do. The speciality of general practice is of equal importance to that of any of the recognized specialities. The words of St. Paul "We are many members in one body, and all members have not the same office" apply very directly to our profession at the moment and for the future. For more than twenty years I have tried to persuade my colleagues in general practice that it is in the interests of pregnant and parturient women, and it is to their own advantage, to hand over obstetric practice to specialists. They usually have obstetric specialists to look after their wives—in one single year I attended the wives of 23 general practitioners. Let me quote from my Inaugural Lecture on February 10, 1927, when I was transferred from the Muirhead Chair to the Regius Chair of Midwifery in Glasgow University:

"The future of general medical practice lies more and more in the direction of *pure medicine*, and the general practitioner must be raised in pure medicine to a very high level. He, associated more intimately with the consulting physician, clinical pathologist, and officer of health, is the individual whose assistance will be of inestimable value in advancing medicine. For, as the late Sir James Mackenzie pointed out repeatedly, on the general practitioner must we depend for the early recognition of disease—the field of medicine which at the present moment offers the most promising harvest. Though this will ultimately be the vocation for the general practitioner, it does not mean that he will occupy a less important place in the community, nor that he will be less beloved than the old-time family doctor. The general practitioner, as I see him, will occupy a more important place, and incidentally he will have an infinitely more interesting professional life." (*Brit. M. J.*, 1927 (i), 870).

Obstetricians are agreed that the ideal arrangement is that maternity hospitals should be units of the general hospital. There are now many examples of this arrangement

in England, Scotland and Northern Ireland—one of the latest to be erected is the Simpson Memorial Unit of the Royal Infirmary, Edinburgh.

The staffing of maternity hospitals or maternity units of general hospitals, and the antenatal clinics associated with them, and the antenatal clinics of local authorities by specialists who will be responsible for both antenatal and intranatal care is simple, for large cities. Very different is the position in respect to small towns and sparsely populated rural areas. For them (and it has been done already in certain areas) it is suggested that the local practitioners should select some of their number for maternity work. These family practitioners selected would be expected to undergo special post-graduate training and take a diploma in obstetrics.

Obviously the administrative bodies of the "region"—presumably the country will be divided into "regions"—will be the local authorities of the region with the Ministry of Health as the "Central Directing Body". Agreement in respect to the constitution and personnel of the "Regional Bodies" will probably be reached comparatively easily—indeed there has been a good deal of spade work done already by The Medical Planning Commission and other bodies. Time permits me to deal only with the constitution and personnel of the "Central Directing Body".

The arrangement which I personally advocate is an *ad hoc* body at the Ministry of Health and at the Department of Health for Scotland designated "The Central Obstetric Board of the Ministry of Health for England and Wales", and "The Central Obstetric Board of the Department of Health for Scotland". We should not be put off with an "Advisory Committee"—such committees have no authority and in my experience, their views are received with the greatest courtesy, then filed and forgotten in most instances. The "Central Obstetric Board" for England and Wales should be representative of all concerned—Ministry of Health, Regional and Local Authorities, Obstetricians (nominated by the Royal College of Obstetricians and Gynæcologists), General Practitioners (nominated by the British Medical Association), Midwives (nominated by the College of Midwives), and Insurance Commissioners. It might be advisable to include representatives from other bodies. The Board for Scotland would be constituted on similar lines. Personally I favour the view that the Chairman should be the Permanent Secretary of the Ministry or the Chief Medical Officer of the Ministry of Health, and in the case of Scotland the Permanent Secretary or the Chief Medical Officer of the Department of Health. Some might prefer an independent Chairman; but there are obvious objections to that arrangement. My scheme for a National Maternity Service was published in the *Journal of the Royal Sanitary Institute*, 1931, 52, No. 4, 156.[1]

The views expressed when I presented my scheme are in the main the same as I hold to-day. Every year that passes some come nearer fulfilment. Of one detail I have seen no promise of fulfilment so far, viz. the creation of a "Central Obstetric Board" at the Ministry of Health for England and Wales, and at the Department of Health for Scotland. *That I consider of vital importance* if we are to have a National Maternity Service with all the agencies concerned working together harmoniously.

This gives me the opportunity of referring to concessions which each and all must make to establish the co-operation so freely advocated by individuals from the highest to the humblest in the Public Health Service. I would point out that obstetric specialists, family practitioners, midwives, and voluntary hospitals would make considerable sacrifices should a National Maternity Service be established. They have such an abhorrence of bureaucratic control that one and all hesitate to give it their support. If, however, the Ministry of Health for England and Wales and the Department of Health for Scotland would indicate their approval and support of a Scheme, such as I have suggested, in which the "Directing Body" was representative of all the agencies working the service, objectors to a National Maternity Service might be persuaded to co-operate, and to do so with a certain degree of enthusiasm.

[1] Also as Chapter XVII (page 332) in "Maternal Mortality and Morbidity—A Study of Their Problems" (by J. M. Munro Kerr, E. & S. Livingstone, Edinburgh, 1933). Blair Bell presented a scheme as did also Ministry of Health Interim Report of Departmental Committee on "Maternal Mortality and Morbidity" (1930), and the British Medical Association in its Memorandum on a "National Maternity Service" for England and Wales, published in the *Brit. M. J.*, 1929 (i), Suppl. 258. A very exhaustive review of these four Schemes was published in the *Lancet*, 1931 (ii), 367.

Now in conclusion permit me to digress for a moment or two from Maternity Hospitals and a "National Maternity Service" to the wider question of General Hospitals and a "National Medical Service". Here one of the outstanding questions is: Should Voluntary Hospitals be preserved as definite entities in the hospital services of the country; or should there be unification of voluntary and municipal hospitals and one type of hospital established?

I am well aware that there is a large and influential body of opinion in favour of preserving voluntary hospitals; but there is also a large body of opinion in favour of *unification of hospitals* at the earliest possible date—obviously impossible at the moment! We, for I include myself amongst the latter, consider that it is an anomaly to have two types of hospital doing the same work. We think it is inevitable that comparisons will be made regarding their respective services in general and in particular regions. We believe that the standard of efficiency in modern municipal hospitals is no whit below that in voluntary hospitals—take as an example the results in the maternity units of the L.C.C. hospitals. Speaking for myself I served all my medical life in voluntary hospitals, except for one year when I was one of the R.M.O.s in the large Fever Hospital (Belvedere) on the outskirts of Glasgow. The standard of medical work and nursing has always been of an extremely high order in this hospital, and it has had some very distinguished medical superintendents.

To witness the passing of Voluntary Hospitals will be particularly sad for us who have served or are serving in them. We can understand also the regrets of Chairmen, Governors, subscribers, and many others who have ungrudgingly given of their time and substance to maintain these wonderful institutions.

I am under no illusion that any words of mine, or of others of a like opinion, will have any influence in preventing an attempt being made to maintain voluntary hospitals as distinct units of a National Hospital Service. Already a *most* complicated machinery of Divisional and Regional Councils for furthering this object is being set up. Each will have its subcommittees, special committees, *ad hoc* committees and so on. It is, I admit, quite impossible to carry on any public service without committees and subcommittees; but let us try to cut down and simplify as far as possible this Committee work, which clogs the wheels of progress and wastes the time of men of ability and action.

I have permission from Sir Frederick Menzies, K.B.E., F.R.C.P., to quote from a letter received a few days ago.

"My dear Professor,

"In reply to yours of the 6th, I should unhesitatingly agree that the *ideal* arrangement is *one* Hospital Service for the whole country, and provision in such a service for all classes of the community; and payments for the same in accordance with 'capacity to pay.'

"But, and unfortunately it is a great big 'But'—the attainment of such an ideal is, at all events at the moment unattainable. All history goes to show that *progress in this* country is by a process of *evolution* and not revolution. *War conditions tend to expedite the process of evolution in some respects at all events.*

"It seems to me, therefore, that these two conditions: (*a*) the inevitable changes in the voluntary hospitals and (*b*) the changes for the better in municipal hospitals will combine ultimately in the merging of the two types of hospital service into one—that is to say—Your ideal will come about by a natural process."

One group of hospitals colloquially designated "Teaching Hospitals" should be given special consideration in any scheme for a National Hospital Service. Obviously that is too controversial a question to discuss in this Address. Conceivably they might be retained as definite units and subsidized by grants made by "The University Grants Committee".

While we are slowly progressing to a "National Medical Service" for insured persons with incomes up to £420 per annum (possibly up to £500 per annum in the near future), *and their dependants*, might it not be advisable that members of the medical profession give consideration not only to the "regional organization" but also to the "central body" at the Ministry of Health, which will direct the service?

I have quoted from St. Paul, now let me quote the words of St. Matthew: "Agree with thine adversary quickly whiles he is in the way with you." I do not mean to suggest

that The Ministry of Health is an adversary of the medical profession in the literal sense of the word; but I do state that it is an autocratic body—I wish it to be *more democratically constituted for dealing with matters that directly concern medical practitioners (family practitioners and specialists alike), who after all do the great bulk of medical work.* The "Central or Controlling Body", I have suggested for a "National Maternity Service" might be created in triplicate, so dear to officialdom. Thus we might have a *Medical* (including the Medical Specialities) Board a *Surgical* (including the Surgical Specialities) Board and an *Obstetric* Board—each constituted on lines such as I have indicated for obstetrics—within the Ministry of Health under the Chairmanship of the Permanent Secretary and the Vice-Chairmanship of the Chief Medical Officer of the Ministry, and with one representative from each of the three Boards and from the body of general practitioners in the Ministry additional to the Chief Medical Officer of the Ministry of Health. There is an "Advisory Medical Committee" associated with the Ministry and there is the "Board of Control" loosely associated, but independent of the Ministry. Thus there exists already bodies containing the foundations of "a directing body" such as I have suggested.

But while I am convinced that such an arrangement is ideal for Obstetrics I am not prepared to stress it for Medicine and Surgery. I leave Physicians, General Practitioners and Surgeons to indicate their wishes.

It is of vital importance that the State has whole-hearted co-operation from the medical profession in its National Health Service.

Cases were reported and specimens shown at the meeting as follows:

Miss Gladys Hill: An Unusual Uterine Tumour.

Miss M. Moore White: Two Cases of Sarcoma of Uterus. Report of case of spontaneous delivery following course of radium therapy for recurrence of epithelioma of vulva when patient two months' pregnant.

Photographs and sections of epidermoid carcinoma of cervix showing extension to body of uterus. Slides of ovarian cyst containing granulosa-cell tissue in wall. Slides of solid ovarian tumour. ? Anaplastic carcinoma. ? Spindle-cell sarcoma.

Mr. J. V. O'Sullivan: Case of irreducible prolapse, complicated by stones in the bladder.

Section of Dermatology

President—H. C. SEMON, M.D.

[*January* 15, 1942]

Erythroplasia.—CLARA M. WARREN, M.R.C.S., L.R.C.P.

Examples of extra-mammary Paget's disease are rare, and this one in a man of 66 shows many typical features. The initial lesion was said to be an infected fissure on the dorsum of the penis, first noticed about four years ago. There was difficulty in getting the area to heal, and it has relapsed at intervals, the erythema gradually spreading until half of the circumference of the organ is now involved. It is well marginated; the centre shows some atrophy, and subcutaneous thickening is palpable, particularly at the periphery. The Wassermann reaction is negative. The diagnosis was confirmed by microscopical examination.

Discussion.—Dr. W. FREUDENTHAL: A biopsy shows a moderately irregular acanthosis with a few clumping cells of the Bowen type. The histological findings in cases of erythroplasia vary greatly.

The PRESIDENT: Has anyone seen a case in which the glans escaped? And what is the prognosis here?

Dr. JOHN FRANKLIN: For treatment the best chance of getting a good result short of surgery would be contact X-rays.

Dermatitis Atrophicans (Atypical).—J. E. M. WIGLEY, F.R.C.P., and W. FREUDENTHAL, M.D.

An apparently healthy man, aged 20, with no history of previous skin disease. The present lesion on the left thigh has been noticed about five years, whilst those on the right arm and lower legs have been present about four years. He does not know the duration of the small lesion on the right thigh. The lesions are symptomless, though he admits there may have been occasional very slight itching. He says he feels perfectly fit, and was only discharged from the Army this year as the skin lesions were diagnosed as lupus. He has never had X-ray treatment. W.R. is negative.

The two principal lesions are those on the inner side of the right upper arm and the outer side of the left thigh. Each is about the size of the palm of the hand and of irregular oval shape.

The lesion on the right upper arm is an ill-defined area, showing a wrinkling of the skin suggestive of superficial atrophy, some sparse scaling, telangiectasis and irregular pigmentation. There are a few red papules scattered over the areas and the whole

appearance is strongly reminiscent of a chronic X-ray dermatitis, being also suggestive of poikilodermia atrophicans vasculare (Jacobi).

The lesion on the outer side of the left thigh is more sharply defined and the atrophy is more marked. There is considerable loss of substance, producing a saucer-like depression, about 4 by 3 in. in area and up to ⅓ in. deep, and the larger vessels are easily seen through the wrinkled skin. The pigmentation is well marked and there are one or two scabbed lesions which look like the result of trauma (e.g. scratching).

The lesion on the right thigh is an ill-defined slightly atrophic area, in which a definite "gap" can be felt in the substance of the skin on palpation. The other lesions are similar in appearance (though smaller) and give the impression of being intermediate between those already described. The total number of lesions is 5.

Biopsy A. (from the lesion on the right thigh): The special features are regressive connective tissue changes in parts of the deep cutis and in the strands between the fat lobules. The normal, thick collagen bundles are mostly replaced by very fine connective tissue fibrils which form a close, irregular network. Most of the fibrils stain distinctly red with van Gieson, others only very faintly. The elastic fibres in these parts are greatly diminished. Regressive changes are also seen in adjacent areas of the subcutis where the meshes of the fat tissue are torn and stain faintly.

Throughout the cutis there is a considerable, mainly perivascular round-cell infiltrate. The walls of some of the vessels are greatly thickened. In the areas where regressive changes are seen, however, the infiltrate is almost entirely absent.

Biopsy B.: A small, flat, red, shiny papule, 1 in. from the saucer-like depression on the left thigh. There is a fair amount of round-cell infiltration, diffusely arranged in the papillary body and perivascularly in the middle and deeper cutis. Within the infiltrate the elastic fibres are diminished. No regressive changes in the connective tissue.

Comment.—The case is one of primary or essential atrophy of the skin. Although it does not appear to be identical with those already described either as poikilodermia atrophicans vasculare or acrodermatitis atrophicans it has some clinical characteristics of each of these. It is therefore recorded as dermatitis atrophicans (atypical) as we think it is better than to add to the already numerous names of the subdivisions of primary atrophy.

Dr. ST. R. BRÜNAUER: This case shows clinical signs of different types of skin atrophy. On the right upper arm there is an area of scaly, cigarette-paper-like atrophy, the surroundings of which show subacute redness. Changes of such a kind mostly occur in cases of diffuse atrophy of the skin. On the outer part of the left thigh there is a larger area of deeper atrophy with the inner parts slightly depressed. Here and there near the atrophic areas small, flat papules of bright red colour are to be seen as they were described by Holoussi Behdjet of Ankara as primary lesions of poikilodermia vasculare atrophicans. Telangiectasis and pigmentation which are signs of poikilodermia atrophicans vasculare as well, are to be found in nearly every one of the atrophic areas.

It might well be that this remarkable case is a transitional kind of atrophy to be placed between the diffuse idiopathic atrophies and the poikilodermia atrophicans vasculare.

Tuberculosis Verrucosa Cutis and Lichen Planus.—W. N. GOLDSMITH, M.D.

L. P. W., man aged 51. Chauffeur.

Present condition (25.11.41).—The right palm is contracted and covered by a hard warty plaque with mauve border. On both forearms are small irregular purple scaly infiltrated patches. Some look like lupus vulgaris, and others having a whitish flat surface, rather more like lichen planus. Those tested with a matchstick did not give the usual sign of lupus vulgaris.

History.—The eruption on his forearms is of two and a half years' duration. Twenty years ago he had a compound ganglion (probably tuberculous) removed from his right palm. The present appearance of the skin of the palm developed gradually. His general health is good and there is no tuberculosis in the family.

Investigations.—W.R. negative. Skiagram of the lungs shows extensive active tuberculous changes.

Biopsy (Two sections were shown under the microscope, prepared and examined by Dr. Freudenthal).—A nodule looking like lupus was removed from the right forearm, and one suggestive of lichen planus from the left forearm. Microscopically the former showed several sharply demarcated foci of tuberculoid tissue with necrotic centres, and at the periphery were smaller foci of epithelioid cells. These were separated from the epidermis by a narrow strip of normal connective tissue. This histological picture is characteristic of lupus vulgaris and is never met with in lichen planus.

The other specimen (from left forearm) presented the typical histology of lichen planus without a trace of tuberculoid tissue. It showed hyperkeratosis, granulosis, and acanthosis. A small-celled infiltration, sharply limited below, runs along the upper part of the cutis. There is also a group of colloid blocks of the same shape and arrangement as depicted in Kyrle's illustration of lichen planus ("Histo-Biologie der Menschlichen Haut und Ihrer Erkrankungen," Wien: Springer, 1, 186, fig. 108). Such colloid blocks are seldom seen in any other disease.

Comment.—At my first clinical examination I was doubtful whether the diagnosis was tuberculosis verrucosa and lupus vulgaris, or lichen planus et verrucosus. It is not easy clinically to pick out which lesion is which, but the histology leaves no doubt that both diseases are present. It is remarkable that they should both be confined to the same regions.

The case, as pointed out by Dr. Freudenthal, is of some significance in connexion with the nature of lichen nitidus. It has been suggested that this might be lichen planus which provokes a tuberculous type of tissue reaction when it occurs in a tuberculous subject. But here we have lichen planus maintaining its own peculiar histology in close juxtaposition with tuberculosis of the skin.

Discussion.—Dr. H. W. BARBER: Is the condition of the palms tuberculous, or is it lichen planus?

Dr. GOLDSMITH: I should expect it to be tuberculous. There is a history of the removal of a multiple ganglion. The condition of the overlying skin has developed from that operation wound for twenty years, quite gradually spreading—so gradually that the man took no notice of it.

Though no tubercle bacilli were found a skiagram showed tuberculous changes in the lungs.

Dr. GRAY: I think that it is extremely difficult to distinguish between the lesions on the right forearm and those on the left. I should have said that whatever was the histology, the lesions were the same on both. I suggest more pieces be examined. I think that where lesions are clinically the same but differ histologically one should not be satisfied with one histological examination.

Cellular Nævus Resembling Lupus Vulgaris.—GEOFFREY DUCKWORTH, M.R.C.P.

This case is interesting because it has been mistaken for and treated as lupus vulgaris for many years. The patient is a healthy girl aged 19. At 8 years one or two papules appeared, followed by others. The present lesion gradually developed on the chin-strap area of the right side of the neck, extending from the angle of the jaw to the mid-line, in front, where it stops abruptly. It is an oval patch, made up of discrete reddish-brown papules and nodules, that show a brownish-yellow staining on glass pressure. Wrinkling of the epidermis is present and slight atrophy is to be seen, but nowhere is this localized—it is spread diffusely over the patch. Presumably this is due to the treatment which has consisted of a few applications of chemical caustics and many of ultra-violet light, given locally. Histology: Sections show a cellular nævus, pigmented in places.

Discussion.—Dr. J. E. M. WIGLEY: Whether the condition is lupus or a nævus could not excision with subsequent grafting be undertaken? Then one could obtain many sections.

The PRESIDENT: I remember a recurrence in the scar after excision for which the patient was X-rayed several times. He then came under my care and I sent him to Professor Rollier who failed, however, to do any good whatever with solar therapy, and explained that the X-ray treatment had spoiled his chance of getting a good result. I have always been averse to excision of lupus vulgaris on the face.

Dr. H. W. BARBER: Dr. Whitfield was in favour of excising patches of lupus vulgaris when practicable, but emphasized the necessity of removing the underlying subcutaneous tissue. I believe that Mr. Arthur Edmunds obtained excellent results in several cases referred to him by Dr. Whitfield.

Dr. A. M. H. GRAY: That is true where there are patches of lupus in such positions that free excision is possible. In such cases, after taking away the fat underneath, a recurrence is rare. The story is very different in the case of lupus on the face.

? Epidermoid Tumour of Nævoid Origin.—GEOFFREY DUCKWORTH, M.R.C.P.

Male, aged 63, A.R.P. worker. Has complained of an intensely itchy patch over his right shoulder-blade for two years. Clinically, the lesion is benign; pathologically, from the limited evidence available, possibly malignant.

On examination.—There is a circular patch, about an inch in diameter, of lichenification, situated over the upper part of the right interscapular region. There is a marked infiltration of the skin. It is circumscribed, and freely movable over deeper parts.

The patient does not remember having had a mole or other blemish on the affected part of the skin. The W.R. is negative.

From examination of the small piece of tissue removed for biopsy a positive diagnosis seems scarcely possible. The section shows, in the corium, well-defined epithelial cell masses, made up of prickle cells externally and horny pearls centrally. No basement membrane is present. There is a varying degree of cellular infiltration in the corium between the clusters of epithelial cells. The epidermis is acanthotic, shows a well-marked granular layer, and is moderately hyperkeratotic, especially at the mouths of the pilosebaceous follicles.

The possibilities seem to be: A prickle-celled epithelioma, perhaps taking origin from a small sebaceous cyst, or wall of a hair follicle; or an epidermoid tumour of nævoid origin.

POSTSCRIPT.—Microscopical examination of the nodule after its excision showed epidermal changes consistent with the clinical findings of lichenification. In the dermis there were many small and a few larger cysts with epidermoid walls, resembling sebaceous cysts of nævoid origin. Malignant proliferation appeared probable in one part. There was some perivascular cellular infiltration.

Myxœdema Papulosum et Annulare.—W. FREUDENTHAL, M.D., and ST. R. BRAÜNAUER, M.D.

E. A. R., clerk, aged 39. Has always been in good health, except for a "fit of giddiness" in March 1933 when a high blood-pressure was found. Later on he had two or three similar but slighter attacks. In July 1934 lesions appeared on the backs of the hands and wrists. In the following years they spread very slowly to the arms, trunk and legs. In recent months a great number of fresh lesions have appeared as we have seen in the last ten weeks while he has been under our observation. These lesions are symptomless except for slight itching and reddening on exposure to sunlight.

Present state: Hundreds of lesions are present on all parts of the body except the face, palms and soles. They are particularly numerous on the back and arms. The initial lesion is a small dome-shaped papule which slowly increases to 6-8 mm. in diameter. Papules larger than this may become dimpled in the centre and, with increasing size (12-15 mm.) form small rings with apparently normal centres. In all stages of development—papule, dimpled papule and ring—the lesions are very soft; their colour is that of the surrounding skin or slightly paler, looking somewhat opaque. In a few places, e.g. the wrists, some lesions have regressed and left ring-like vestiges and a very superficial scarring.

A biopsy of a papule showed a large amount of mucin especially in the uppermost part which was covered by an epidermis with rete pegs flattened by pressure. Mucin was also present below the papule, the amount gradually decreasing towards the middle and still more, towards the deep part of the cutis. A biopsy of an annular lesion showed a fair amount of mucin in the area of the ring or a little below, in the central part there was only a little mucin left, but there was some round-cell infiltration.

Internal examination revealed an adenoma of the right lobe of the thyroid gland, with deviation and compression of the trachea from which the patient at present suffers no discomfort. Mr. K. Eden suggested the removal of the tumour.

Numerous dome-shaped papules on the back. A few, in the right lower corner, show some dimpling. (For another photograph of this case showing annular lesions, see report of this meeting in *Brit. Journ. Dermat.*)

Comment.—Three groups of cases of myxœdema might be distinguished: (1) The classical generalized myxœdema of cretins (Gull and Ord). (2) The pretibial myxœdema, especially in Graves' disease. Cases (after thyroidectomy) were shown at previous meetings (Dowling, G. B., *Proc. Roy. Soc. Med.*, 1934, **27**, 1361; Bamber, G. W., *ibid.*, 1937, **31**, 350). (3) The "atypical" myxœdema of Jadassohn-Doessekker (Doessekker, W. *Arch. f. Dermat. u. Syph.*, 1916, **123**, 76), with a great variety of skin manifestations: circumscribed or, like our case, disseminated or eruptive, tuberous, plaque-like, lichenoid, papular, fibromatoid, &c. With increasing knowledge we should soon be able to classify these "atypical" cases. A connexion with thyroid dysfunction is usually less obvious in this group than in the two others and is sometimes only shown by the involution of the skin lesions after administration of thyroid or, as in Jadassohn-Doessekker's case, after implantation of thyroid tissue.

Discussion.—Dr. St. R. Brŭnauer: This case is almost unique. Similar cases in the literature do not show such numerous lesions all over the skin, nor the presence of papulo-lenticular, dimpled or umbilicated, and annular lesions in the same case.

Mr. Kenneth Eden: This patient had a small nodular goitre, but no evidence of thyrotoxicosis or myxœdema, the basal metabolic rate being normal. I have never seen a case of this type before.

Dr. Trotter and I have, however, been interested for some time in localized myxœdema associated with thyrotoxicosis. At a thyroid clinic during the last three years, we have observed three cases of circumscribed pretibial myxœdema with toxic diffuse goitre in a series of 134 cases of toxic diffuse goitre and 254 cases of goitre, so that the incidence of this skin disease is not apparently insignificant in toxic diffuse goitre.

The first of these cases was the most obvious, developed before the thyrotoxicosis was treated, and persisted after treatment. The second case was less obvious, and the skin plaques first appeared eight months after thyroidectomy when the disease was quiescent. The third case had only a slight degree of the condition and was noticed before operation, only because we were looking for it. In the last two cases the plaques have tended to disappear spontaneously over a period of many months.

The association of this pretibial type of localized myxœdema with thyrotoxicosis is a feature of all the recorded cases, and we have been chiefly interested in this apparently paradoxical association. Unfortunately so far we have not found the explanation, though we have assured ourselves that the skin condition does not respond to treatment with thyroid extract, and apparently pursues an independent course. In addition, biopsies of the pretibial skin in other cases of Graves' disease have shown no excess of mucin.

Dr. Freudenthal's case is different from the pretibial form, but it is interesting to find that although thyrotoxicosis is absent there is some evidence of thyroid disease. I think the adenoma should be removed in view of the tracheal obstruction and this will provide histological evidence to complete the case.

Dr. GORDON: Is the distribution of mucin in this patient the same as in the pretibial myxœdema of the skin?

Dr. W. FREUDENTHAL: In pretibial myxœdema mucin is found mostly in the middle and deeper parts of the cutis and subcutis, although sometimes, e.g. in warty lesions, it may also be seen in the upper part of the cutis.

Mr. KENNETH EDEN: In the article on this subject (Pillsbury, D. M., and Stokes, J. K., *Arch. Dermat. & Syph.*, 1931, **24**, 255), two forms of localized myxœdema are distinguished. One is the pretibial plaque-like form, and is always associated with thyrotoxicosis; the second is nodular, and is unassociated with obvious thyroid disease. It is possible that Dr. Freudenthal's case might fall into the second group.

Lichen Simplex Controlled by Stilbœstrol.—H. C. SEMON, M.D.

A woman, aged 47, has had lichenification of the right thenar eminence with pronounced itching on and off for twenty years. There are no lesions elsewhere. After hysterectomy three years ago there were menopausal flushings until recently. She was first seen by me on October 27, 1941, and was treated with 1 mg. tablet of stilbœstrol daily for ten consecutive days in each month. The cutaneous symptoms (and the flushing) appear to be controlled without local applications of any kind.

Scleroderma Circumscriptum.—H. C. SEMON, M.D.

This patient gave a history of two years' pruritus vulvæ, with a "feeling of dryness". She also complained of frequency of micturition, without stress. Menopause nine years previously, at the age of 39. She had previously been treated for an ulcer at the junction of middle and lower third of front of left leg, which had been labelled provisionally "? tuberculous". The Wassermann reaction was negative. Cervix and uterus: nothing abnormal. There were redness and induration around the vulva and on adjoining skin of both thighs, with atrophy of the labia and contraction of vaginal inlet. This is tight posteriorly and cracks on examination.

The most active and troublesome of the lesions in this case are on both sides of the vulva, which is itself involved in the cicatrizing process. The patches here are circumscribed and show marked atrophy. There is a rough symmetry. Additionally there is a small brooch-like lilac ring type of lesion on the front of the right side of the chest, while the skin above and behind the right shoulder displays the type known as "white spot" disease. The white patch on the front of the left leg has undergone ulceration, as not infrequently happens over bony prominences as a result of trauma. Some relief of the pruritus appears to have followed the administration of stilbœstrol *per os*.

Tuberculosis Nodularis Cutis with Glandular Involvement.—H. C. SEMON, M.D.

The patient has complained of cough, palpitation, and feeling tired for a number of years, and Dr. Lisle Punch reported "arteriosclerosis with myocardial degeneration and cardiac failure". The Wassermann reaction was negative, and an X-ray of the chest revealed cardiac enlargement and pulmonary congestion and hilar shadows "reported as being glands". Several soft elastic glands were palpated at that time in the neck and in the right axilla, but the spleen and liver were not palpable and a blood-count was normal—Hb. 98%, W.B.C. 7,000. In November 1941 there was "great enlargement of all accessible lymphatic glands, liver slightly palpable, spleen not palpable, enlarged heart, congested pulmonary bases with signs suggestive of obstruction by hilum glands, also purple subcutaneous nodules on both arms and on the trunk. These nodules are apparently increasing in number, and they are said to vary in size and to become less noticeable on holiday. Some of them show reduced sensitivity to pin-prick and cotton-wool. They have been observed by the patient for the last eighteen months".

No history of tuberculosis.

The patient feels languid, cannot concentrate, sleeps badly, coughs a lot. Sputum scanty, never hæmoptysis. He is gaining weight. Marked breathlessness on exertion.

All accessible glands enlarged, but not tender or painful. The upper extremities symmetrically involved on extensor aspects. The back shows similar though less marked lesions of one type only: nodules of a bluish purple colour of various sizes from a pea to a large plum. They all involve both the epidermis and the hypoderm, from which they appear to take their origin. Their distribution on the extensor surfaces strongly suggests a lymphatic spread. On the back they are situated mainly on the flanks in the lines of cleavage. There is no tendency to ulceration, while on the upper arms they are undergoing a definite shrinkage and tendency to involution.

Histology of skin lesion displays a tubercular structure with sparse giant cells and a rather degenerative tendency of both nuclei and cells. A second slide reveals acid-fast granules and bacilli in moderate number.

Blood examination (Dr. K. M. MacLaren): R.B.C. 4,600,000 per c.mm.; Hb. 94%; C.I. 1·0; W.B.C. 7,000; polys. 42%, 2,940 per c.mm.; lymphos. 41%, 2,870 per c.mm.; monos. 8%, 560 per c.mm.; eosinos. 9%, 630 per c.mm.; basos. nil.

The case had been diagnosed as leprosy, but with the exception of a single cruise as far as Italy the patient has never been out of the country. My own feeling was rather against that diagnosis. On biopsy of one of the nodules on the forearm we were surprised to find acid-fast granules and also quite a number of acid-fast bacilli. The generalized adenitis which this patient has would, I think, be rather against a diagnosis of leprosy and more in favour of a tubercular manifestation. One member suggested sarcoid, another Hodgkin's disease with skin manifestations; both these diagnoses were rather upset by the finding of the acid-fast bacilli. Dr. Gray has suggested that we remove a gland and inject into a guinea-pig to settle the diagnosis as between leprosy and tubercle.

Discussion.—Dr. W. FREUDENTHAL: A skin biopsy shows a large amount of sarcoid and tuberculoid tissue with a very small number of acid-free bacilli. There are also acid-fast granules present. These alone, however, should always be interpreted with caution in skin sections, as normally sweat glands contain acid-fast granules. This fact was not sufficiently known, so these granules had been mistaken for the granular form of tubercle or leprosy bacilli.

Dr. A. M. H. GRAY: This case appears to be one of a very definite group of cases which apparently are tuberculous. It is very similar to two others I have seen. At first glance this case looked like a sarcoid, but the glands are enormous for sarcoid, and the histology and the finding of bacilli seems to be against it. There are two things to be noted: the very large glands and the fact that they were present for a long time before skin lesions appeared. That suggests a Hodgkin's disease on the history. A woman came to me at University College Hospital with a huge mass on one side of her neck; she had had it for eleven years. She then developed a patch of lupus on the right side of her face of very much the same type as in this case, and this has gone on spreading in spite of treatment over a considerable number of years—eight or nine. We clear up one patch by one method or another, and then fresh nodules of the same type come up at the periphery. She has lost practically the whole of her ear on the right side, as well as considerable facial tissue. The second case was seen at

Great Ormond Street. A child came up with huge glands all over the body. A diagnosis of lymphadenoma had been made. It proved to be lupus of the hypertrophic type, associated with the pre-existing general adenitis. The case now shown is, I think, of exactly the same type—apparently a case, not of Hodgkin's disease but of true tuberculosis.

Bullous Livedo from Heat.—E. W. Prosser Thomas, M.D.

Mrs. E. H., aged 42, complaining of blisters on legs on and off for five years. Eruption comes in attacks lasting about six weeks. Blisters leave behind pigmentation. Present attack has lasted four weeks. She had three attacks in past year. Has had similar blisters on the back of the right lower forearm, otherwise no other part of the body has been affected and there has been no previous skin trouble. She ascribed the original outbreak to her occupation, raking out fires, the areas involved being those most exposed to heat.

On examination.—Numerous thin blisters containing clear serum are present over the inner aspect of the left leg and the outer aspect of the right leg. A few have erythematous bases but the majority seem to arise in and to follow the outlines of a livedo reticularis-like background. There is also a good deal of light brown pigmentation in the affected areas apparently from healed blisters. There is a similar faint reticular pigmentation over the lower extensor surface of the right forearm. In view of the distribution of the lesions over the right sides of the legs and the back of the right forearm, her explanation that heat is responsible seems reasonable. Adamson (*Brit. J. Dermat.*, 1916, **28**, 281) in a paper on livedo reticularis mentions a chronic vesicular form due to heat and shows an illustration of a large blister of the leg on a livedo background.

In the present case, however, some of the attacks do not seem to have been associated with fire-raking and have occurred in the summer, which is difficult to explain.

Section for the Study of Disease in Children

President—A. G. MAITLAND-JONES, *O.B.E.*, M.D.

[*January* 23, 1942]

DISCUSSION ON INTRACRANIAL INJURIES IN CHILDHOOD

Mr. D. W. C. Northfield: My experience of cases of head injury in children, has for the most part been acquired since the outbreak of war. Although the air-raid casualties are included, the majority of the injuries have resulted from ordinary accidents and have an immediate application to everyday practice.

The series includes 43 cases, the ages ranging from 3 months to 14 years. In 35, the injury was closed, and of these 11 were air-raid casualties. 9 of these closed injuries were cases of scalp wound—without a break in the underlying bone. The remaining 8 cases had sustained a compound fracture of the vault—that is to say the damage to the brain was of an open variety, with a real risk of intracranial infection. This is the main reason for separating head injuries into "closed" and "open" groups. Cases of scalp wound could be classified as "open", but I regard them as virtually closed—though needing proper surgical attention. Of these 8 cases of compound fracture, 6 were air-raid casualties, a higher proportion than in the case of closed injuries—which is only to be expected.

Analysis of the 35 closed injuries.—There were nine scalp wounds. In 10 cases there was a large hæmatoma of the scalp, a frequent condition in children. This presents as an extensive fluid swelling under the scalp, usually tender to the touch; within a day or so its edges become indurated so as to simulate, in textbook fashion, a depressed fracture. This difficulty can often only be settled unequivocally by an X-ray. The condition in my opinion is rarely found in adults, the reason being the greater fragility of the child's skull. A fracture of the vault of the skull was revealed by X-rays in 15 cases, nearly one-half of all the cases of closed injury, and a much higher proportion than in corresponding adult cases. Of the 10 cases of cephalhæmatoma, a fissured fracture (not depressed) of the bone in the region of the effusion of blood was proven in 8. It was possible to demonstrate radiologically a fracture of the base of the skull in only 1 case, in which there was also clinical proof—a discharge of blood and of cerebrospinal fluid from the ear.

There was an acute brain injury in 26 cases; the criteria employed in making such a diagnosis fall into three groups—unconsciousness, abnormal neurological signs, and symptoms of disturbance of cerebral function. Although these groups will first be considered separately, a given case might have satisfied any or all of the criteria.

In 14 cases there was definite proof of *loss of consciousness*, about which certainty is even more difficult in children than in adults. The child may be playing alone, or with friends too young to give correct information; where the patient is transferred from another hospital, the information is lacking, usually due to carelessness in recording what may be the most obvious physical sign, or in obtaining the history. Of transient unconsciousness it may be impossible to obtain the desired evidence in the rush of rescuing and evacuating air-raid casualties. Failing a reliable witness of loss of consciousness, traumatic amnesia of the incident has been accepted as equivalent evidence, and probably more than 14 of the patients lost consciousness. 7 of these cases sustained a fracture of the skull. A point to be referred to later is that among the 15 cases of fractured vault, there were 10 in which consciousness was apparently not lost. Loss of consciousness varied in degree and duration; in some cases it was only for a minute or so, but in the most severe the patient was unresponsive for hours, delirious and uncooperative for several days

Abnormal neurological signs were found in 9 patients. These signs always disappeared, and usually rapidly.

The commonest feature of acute brain injury was the group of symptoms which in the adult are associated with a major cerebral contusion, namely *headaches, irritability and resentfulness, drowsiness and vomiting*. These occurred in 16 patients, for periods varying up to a maximum of fifteen days.

When one or more of these clinical criteria of acute brain injury was present in the same case, the common combinations were unconsciousness and symptoms, 6 cases; signs and symptoms, 6 cases; and symptoms only, 6 cases. In 3 cases unconsciousness was followed by neither signs nor symptoms, and in 2 by signs and no subsequent symptoms. There were 3 cases in which the complete triad of unconsciousness, signs and symptoms was present, and 2 of these were very ill children. There was one other severe cerebral injury making only three in all for the total 35 cases of closed injury, a very small proportion when compared with adult cases of injury.

The immediate prognosis was excellent. None died, and all recovered speedily. Some stayed in hospital for only one to two weeks, the most severely injured stayed for three months, but that was due more to the difficulty of finding him appropriate accommodation than to unusually slow recovery, which was interrupted by an acute appendicitis.

Analysis of eight open injuries.—There have been 8 cases of compound fracture of the skull, and as already stated, the scalp wounds with no underlying fracture are included in the series of closed injury, as is a case of fractured skull-base although technically compound. Air-raid incidents have been responsible for the injury in 6 cases. The fracture has occurred over any region of the vault and due to a blunt object or to a missile, the dura mater being penetrated in 4 cases, and there has been a varying degree of damage to the underlying brain. In 3 of the cases there was loss of consciousness, and in 3 there were signs of brain damage. In only 2 were there the symptoms of a major cerebral contusion. These cases, though too few to analyse, are in keeping with one's experiences in all head injuries, namely, that in a case of open injury there is commonly no disturbance of the nature of a general cerebral injury, and that if there is loss of consciousness or other evidence of a general disturbance of cerebral functions then the injury is indeed a very grave one, out of all proportion to the degree of damage as judged by the external wound. Abnormal neurological signs are more likely to be found, and are more likely to be permanent, because of the focal nature of the damage to brain beneath the fracture. 2 of these cases of open injury died; 1 from intracranial hæmorrhage in spite of operation—a metal fragment passing through both frontal lobes. The other child died from streptococcal septicæmia, after a very long illness; the organism gained entrance through a compound depressed fracture in the occipital region.

Sequelæ.—The follow-up of these cases of children has not been so thorough as in the case of adults, possibly owing to problems of evacuation, and to death of parents. 18 cases have reported for examination for periods up to a year after the injury, and 1 case

watched for five years will be referred to when epilepsy is considered. Of 15 cases of closed injury, 4 still have occasional slight headache at diminishing intervals of weeks; the others are all quite normal except that in 3, the mother complained spontaneously that the child was very restless at night. 1 of 3 cases of open injury has occasional headache.

Epilepsy has occurred in 3 cases, in 2 of which it was focal and motor in character, and developed soon after the injury. One, a baby of 9 months, tumbled from the back seat on to the floor of a car when the brakes were applied suddenly. There was no loss of consciousness or any other apparent disturbance, but a few hours later the left arm was noticed to be hanging limp; about an hour afterwards clonic spasms of the left arm and leg developed and the baby became very drowsy. The arm and leg appeared paralysed. The epilepsy continued on and off for some twenty-four hours, thereafter it ceased, and the arm and leg gradually recovered strength within the next few days. The head appeared normal; a lumbar puncture was attempted unsuccessfully several times. This child (referred to earlier) has been watched for five years and is physically normal, except for occasional attacks of twitching of the left leg. She has taken phenobarbitone throughout this period.

The second case, a boy of 11 years, after six hours' unconsciousness as a result of a bicycle accident, progressed satisfactorily, apart from headaches, for six days. He then developed epileptiform attacks confined to the left side of the body associated with adversive turning of the head to the left. He became very drowsy with virtually complete paralysis of the left side of the body; sensory tests were not possible. The brain was explored through burr holes, on the supposition that there was a subdural hæmatoma. No intracranial hæmorrhage was found but the pia-arachnoid seemed unduly tough and œdematous. Unfortunately I have been unable to keep in touch with this patient.

Both these cases illustrate a well-recognized group, in which epilepsy develops very early after a brain injury, apparently related to an acute disturbance of neural function. Clinical experience supports the belief that this type of traumatic epilepsy may not necessarily persist, and has a better prognosis than the variety which comes on later, with its incidence roughly highest in the second year after the accident, a view favoured by the work of Dennis Williams upon electro-encephalography.

The third case of epilepsy illustrates a different aspect of head injury. A child of 2, injured in an air raid and with a scalp wound, was taken to a hospital. Next morning the child was sent out, the wound having received no surgical attention. The following day, on the advice of the private doctor, the mother took the baby to another hospital where it was admitted, as they discovered and confirmed by X-ray a fissured fracture of the right parietal region beneath the linear wound some 3 in. long. The child when transferred to my Unit four days after the injury, showed no evidence of any brain injury. The scalp wound was exuding pus, due to *Staphylococcus aureus*, and in its depths could be seen the fissure of the fracture. The next day there was a convulsion, not repeated, involving the left arm and face. The wound gradually healed and the child made a complete recovery. Here the epilepsy was due to cortical irritation from a localized patch of pachymeningitis. I quote this case in order to emphasize again that scalp wounds must be regarded as important. A fracture must always be suspected, and surgical attention must always be paid to it. The child with a compound fracture of the occiput, who died of streptococcal septicæmia, received no surgical attention to the wound within four days prior to transfer to my care. The reason offered was that the child was deemed too ill. That was an error of judgment, but too often scalp wounds go septic, and underlying fractures escape detection owing to negligence.

This review points to some conclusions peculiar to head injury in children. The incidence of fissure fractures of the vault in closed injuries is much higher than in adults; and often there is no loss of consciousness, probably owing to the greater fragility of the child's skull, which although probably more elastic, is yet much thinner than the adult's. With the frequency of fracture may be coupled the frequency of cephalhæmatoma simulating depressed fracture. On the other hand, the child tolerates a cerebral injury much better than an adult, and recovers from it much more rapidly and completely. The popular lay notion that "concussion" is a grave condition in a child is not borne

out by experience. It is interesting to speculate on the relationship between these findings and the experimental work of Denny-Brown on acceleration-concussion (Denny-Brown, D., and Russell, W. R. (1941), *Brain*, 64, 93). Both the elasticity of the child's skull and its fragility will tend to block or delay the transmission of the acceleration imparted by the impact, through the skull, to the brain.

There was evidence of mental or psychological disturbance resulting from head injury in only 2 of the cases. One was the case of severe closed injury, in which acute appendicitis occurred. For about three weeks, this boy was petulant, irritable, self-centred and thoroughly difficult; thereafter he rapidly improved and now over a year later he is a normal happy schoolboy. The other patient lost both parents in an air raid, and for a week or so was very quiet and aloof, but gradually thawed and I think his troubles were not directly related to his head injury. The restless nights mentioned by three mothers may be some reflection of a mental stress, not otherwise evident, a small point worth consideration in similar cases.

Dr. W. G. Wyllie: For the most part similar problems present themselves in head injuries in children as in adults. Yet, there are some differences between the young and the mature in their reactions to head injury both in the immediate and in the after-effects. These dissimilarities, and the features which commonly give rise to difficulties in the diagnosis of the different forms of lesion are best illustrated by actual case-histories.

From whatever cause, head injuries at all ages are to be divided into *Open* and *Closed* types. The Open injuries include anything from a minor scalp wound to a compound or a depressed fracture or to cerebral penetration. The grosser forms of Open injury, requiring immediate surgical aid, commonly present, from the outset, signs of focal cerebral damage, provided the injury is not confined to a silent part of the brain.

My remarks are chiefly concerned with cases of the *Closed* type and cases of the *Open* type with minor scalp wounds, with skulls intact radiographically or showing fissure fracture, and with intracranial complications of onset either immediate or delayed for several days. In this group the commonest mode of damage is by violent movement of the head against a solid substance rather than by the sudden impact of a missile against the stationary head. This occurs in civilian practice when babies and toddlers fall out of cots, prams, off beds or chairs, and when older children, chiefly boys lorry-hiking, are knocked down in the street. In this commoner type of head injury these points stand out: the high proportion of cases without scalp wounds, the frequent occurrence of fissure fracture, and the high incidence of concussion.

Fissure fracture.—The first peculiarity of head-injuries in children is the relative ease with which fissuring can occur, frequently without intracranial complications. The cause is a massive diffuse violence as when the head comes forcibly in contact with the ground. When the momentary deformity, chiefly of the vault, reaches the limits of elasticity of the skull, bursting or fissuring occurs. Children's skulls, more elastic owing to their sutural flexibility, might be expected to need more deformity to produce a fracture with consequently a greater likelihood of cerebral damage. Actually, the relative thinness of their cranial bones allows of fissuring under lesser degrees of stress than is the case with the adult. In infants cephalhæmatoma overlying the fracture is common.

A baby girl of 3 weeks had her head knocked against some railings and was then dropped on the pavement. She was stunned, had a mild fit, but showed no abnormal signs except a swelling on the side of the head; she made a good recovery. X-rays showed a long horizontal fracture of the right parietal bone.

A baby girl of 4 months fell out of her pram, was "knocked out", and developed a large fluctuant left-sided cephalhæmatoma; X-rays showed a fissure fracture of the left parietal bone. There were no other symptoms.

CLINICAL FEATURES FOLLOWING HEAD INJURY

Concussion.—Up till recently the rival views on the production of concussion were the *mechanical* or "jarring effect" (Russell) and the *vascular*. The latter, the more popular, did not postulate hæmorrhage but presupposed a sequence of deformity of the skull,

a rise of intracranial pressure, sudden anæmia from collapse of cerebral vessels and loss of function of nerve cells, *unconsciousness*, of short duration. The recent important work of Denny-Brown and Ritchie Russell (1941) on experimental cerebral concussion in animals strongly supports the theory of concussion as the direct effect of physical stress on neurones; they define it as a traumatic paralysis of neural function in the absence of lesions. In the common type of injury with violent movement of the head, *acceleration concussion* is dependent on the changes from primary inertia of the brain to secondary momentum and finally the sudden arrest of momentum of the brain as the skull strikes a hard surface. Acceleration concussion was not found experimentally to be associated with any significant change in the intracranial pressure. In *compression concussion* when the head is fixed and force brought against it locally by striking, concussion was more difficult to produce. *Contusion* these authors outline as the result of physical stress upon the supporting vascular structures with varying degrees of hæmorrhagic effect.

As consciousness is regained in concussion immediate symptoms acceptable as after-effects are a general increased excitability of tendon-jerks, nausea or vomiting, giddiness and headache. Denny-Brown and Ritchie Russell consider that a prolonged state of stupor followed by intellectual impairment can occur as the result of the same mechanism which causes the momentary unconsciousness of concussion and without visible lesions in the brain.

In O'Connell's (1941) 250 head injuries, mostly war casualties (age-groups not given, but mainly adults), of 102 of the *Closed* type, 102 had concussion. In the Closed group it was the concussion which brought them to the neurological unit. In Northfields' 34 closed cases in children, 13 had had concussion. This disparity is due to the manner of selection in the first group and the fewer cases of concussion in children compared to adults owing to the greater elasticity of the skull, though other damage such as fissure fracture may be present.

Vascular and other lesions.—When unconsciousness is prolonged or a lucid interval is followed by unconsciousness or irritation or stupor, the possible causes, difficult to differentiate, include subarachnoid hæmorrhage, contusion (cerebral grazing), cerebral œdema, subdural and extradural hæmorrhages and sepsis. Each has distinguishing features, but in practice the picture is often blurred.

(1) *Subarachnoid hæmorrhage.*—Concussion is not always present, and the onset of headache, drowsiness, stiffness of the neck, pyrexia, unconsciousness may not appear until after an interval of half an hour or so. Slight paralysis is common on the same side of the body as that of the head struck, as the vessels are usually damaged by *contre-coup*. The cerebrospinal fluid is bright red with blood.

(2) *Contusion.*—The lesion is a localized meningo-cortical hæmorrhage either direct or by *contre-coup*. Its presence is suggested by a rapid onset of local paralysis, seldom a complete hemiplegia, provided the injury is not to a silent area of the brain. Jacksonian fits, indicative of the site of the lesion, are likely to develop early in the first one or two days. Only in the more severe grades of contusion is some blood or yellow-staining to be expected in the spinal fluid.

A boy of 1½ years fell from a table striking his head, was not unconscious but apathetic, did not talk and vomited twice. On examination the following morning slight weakness of the right side was found with hypotonicity of the limbs and right extensor plantar response. The cerebrospinal fluid was normal. He made a good recovery.

(3) *Extradural hæmorrhage* by itself would be expected to produce a fairly slow onset of hemiplegia over several days and Jacksonian epilepsy of later onset would favour the diagnosis. In uncomplicated cases the fluid is normal, or yellowish and with a raised protein content.

(4) *Subdural hæmatoma* is usually an encapsulated collection of blood of very slow accumulation. An unlikely result of head injury in children, it occurs at the extremes of life in babies and old people following apparently trivial head injuries.

A case of delayed onset of hæmorrhage, subarachnoid. A girl of 11 months, having fallen from her pram six months and three weeks prior to admission, had attacks of going limp and unconscious with increasing frequency. On admission she was unconscious, temperature 101° F., bulging fontanelle, numerous hæmorrhages, some subhyaloid, in both fundi, but no neurological signs. The cerebrospinal fluid was uniformly and heavily blood stained with an initial pressure of 300 mm. of water. She improved and when seen one month later was in perfect health.

(5) *Œdema of the brain*, probably the commonest complication of all forms of cerebral injury, occurs locally around a traumatic vascular lesion, or at the various poles, but seldom becomes generalized. Symptoms of the cerebral swelling—stupor, irritation, paralyses, unconsciousness—usually appear on or after the fourth day following the injury.

(*a*) ? Œdema. A boy of 6, an air-raid casualty, was concussed for a short period and had an abrasion of the right forehead without visible fracture. Ten days later he again became drowsy, vomited, then unconscious, the pulse-rate being 60-80 for seven days. The cerebrospinal fluid was normal (pressure not estimated). He made a good recovery.

(*b*) ? Œdema and hæmorrhage. A boy of 4 years fell on the back of his head from a roundabout on to concrete. He cried bitterly, was not unconscious, but had severe pains in the back of his head, neck and spine. A transverse fracture of the occipital bone was found. Two days later he walked badly on his left leg, held his head to the left and began to "fall down". The headache was worse and he vomited and was drowsy. After a further two days he had weakness of the left arm as well as the leg. He had six more fits always commencing in the left leg. Recovery has been apparently complete.

(6) *Sepsis*. A case of compound fracture with hæmatomata of the right orbital region and of the scalp in a boy of 10 years. A fracture was not seen but presumably one existed and involved one of the bony sinuses. The boy was not unconscious but restless and irritable, with vomiting, severe headache and pain in the neck. On the day after the accident—a fall from a bicycle—the temperature rose to 104° F. That day on lumbar puncture the initial fluid pressure in millimetres of water was 400; 180 four days later. The cell count in spite of sulphonamides was between 2,090 and 340 for eighteen days, chiefly polymorphonuclear leucocytes; culture: pneumococci. He made a complete recovery.

Pupillary changes in head injuries.—Pupillary inequalities and some degree of nystagmus are often present following a head injury. Apart from bilateral dilatation due to high intracranial pressures these changes need not be interpreted as evidence of pressure or damage to the hemispheres. They depend upon concussion possibly with petechial hæmorrhages in the brain-stem. In violently arrested movement of the head a forceful downward movement of the cerebrospinal fluid can produce petechiæ in the region of the aqueduct, or a contusion of the quadrigeminal plate against the tentorium cerebelli will interfere with normal pupillary functions.

Diagnostic aids. Lumbar puncture.—In all cases at least one diagnostic puncture should be made. In a large proportion of head injuries some blood or staining of the fluid is found and is of little significance unless the quantity is excessive. Then a subarachnoid hæmorrhage is suggested and a lumbar puncture on every second day is advisable.

Much attention lately has been given to pressure estimations of the fluid and to measures of reducing it when high by means of dehydration. My impression is that low readings are more common than high ones but that usually they are within normal limits. High pressures in head injuries are at about a level of 200 mm. of water, and rarely reach 300 mm., not being comparable with the high levels reached in cases of cerebral tumour and meningitis. Ritchie Russell (1932) found no evidence that increased intracranial pressure itself caused death in head injuries. McKissock and Brownscombe (1941) consider that lumbar puncture reduces headache and does not facilitate renewed bleeding, but agree that there is no constant relationship between abnormal clinical signs and the state and pressure of the cerebrospinal fluid.

Ventriculography.—In the later stages of recovery in cases of the *closed* type, if Jacksonian fits develop or local paralysis persists ventriculography can be of great value in determining the need or otherwise of operation.

What are the indications for operative exploration when signs of cerebral damage are present? The view that vascular lesions commonly cause intracranial damage in head injury has been largely altered. Often, when physician and surgeon agree that exploration is needed, no collection of encapsulated blood is found. Local œdema and contusion, more often than bleeding, cause symptoms. Operation should only be considered when signs of deterioration in the patient's condition appear and persist, such as slowing of the pulse and respiration, persistence or increase of local paralysis and Jacksonian fits; or following evidence of ventricular shift revealed by ventriculography.

Sequelæ of Head Injuries in Children

The child escapes the late effects of head injury more than the adult. Headache, so prominent a feature of the post-concussional state in adults, passes off rapidly in the child. A period of reduced mental activity, initiative, or concentration is rare. Most cases on return to school after a sufficient rest do not show scholastic deterioration, possibly because the intellectual processes in the child's brain are less advanced. In cases of more severe injury mental alteration does occur.

A boy of 5 years had a fractured skull from a fall in the road, was unconscious, then delirious and vomited. He appeared to recover after at first dragging his right foot in walking. Two years later he was brought to Great Ormond Street because of screaming fits, nightmares, violent outbursts of temper, being "right out of control", and occasionally going stiff, when he did not recognize his parents. A second X-ray two years after the injury still shows a widely ununited fracture of the right frontal bone. Extradural clot may be present. Here ventriculography is indicated.

The rarity of residual paralyses and epilepsy at all ages, except in penetrating wounds of the skull, is striking considering the degree of change found in the brain in cases of head injury with apparently complete recovery, dying from other causes some time after the injury. Greenfield (1939) has described cortical defects at the summits of convolutions where severe œdema has occurred, and demyelination in the underlying white matter.

Two unusual instances of late sequelæ in children are as follows. Two boys aged 5 and 7 years respectively gave histories of head injury with fissure fractures extending to the base of the skull. Both had initial unconsciousness but made good immediate recoveries. After a period of roughly three months, obesity with bulimia developed in one and diabetes insipidus in the other. The lesions presumably were basal hæmorrhage with slow organization of blood-clot and arachnoiditis in the region of the tuber cinereum and infundibulum.

REFERENCES

Denny-Brown, W., and Russell, W. R. (1941), *Brain*, **64**, 93.
Greenfield, J. G. (1939), *Proc. Roy. Soc. Med.*, **32**, 43 (Sect. Neurol., 1).
McKissock, W., and Brownscombe, B. (1941), *Lancet* (i), 593.
O'Connell, J. E. A. (1941), *ibid.* (ii), 719.
Russell, R. (1932), *Brain*, **55**, 549.

Mr. J. E. A. O'Connell: Dr. Wyllie has pointed out that the incidence of cerebral concussion is considerably lower in Mr. Northfield's group of children with closed head injuries than in a series of patients of all ages referred to by me in a recent paper (*Lancet*, 1941, ii, 719). The real explanation of this difference in the incidence of concussion in the two groups lies in the differing classifications adopted by Mr. Northfield and myself. I have excluded scalp wounds as well as all deeper wounds from the group of closed injuries and consequently all the patients in this group of mine were brought to hospital either because of unconsciousness following a blow on the head or some complication arising subsequently. Obviously patients who had neither a scalp laceration nor a period of unconsciousness after a head injury would be very unlikely to come to a hospital or even to see a doctor.

I believe that pupillary changes after head injuries are of great significance. Unilateral dilatation and fixation of the pupil on the same side as an expanding intracranial lesion has been clearly shown by Reid and Cone to be due to the herniation of the hypocampal gyrus through the tentorial opening with stretching of the oculomotor nerve beneath it. After injury such pupillary changes are of the greatest value in localizing an intracranial hæmorrhage which will be on the side of the dilated and fixed pupil.

Section of Laryngology

President—E. D. D. Davis, F.R.C.S.

[*February* 6, 1942]

DISCUSSION ON THROAT AND NOSE MANIFESTATIONS OF BLOOD DISEASES

W. M. Mollison: The diseases chosen for consideration are: (1) Bleeding of the newborn. (2) Essential thrombocytopenia or purpura hæmorrhagica. (3) Polycythæmia vera. (4) Hæmophilia. (5) Hereditary telangiectasia or Osler's disease. (6) Agranulocytosis. (7) Leukæmia. (8) Achlorhydric anæmia. (9) Avitaminosis. (10) Glandular fever. Though the first three of these diseases exhibit bleeding from the nose and gums, in the absence of any local cause the pædiatrician takes over the case.

(4) *Hæmophilia* has generally declared itself in the boy before the laryngologist is consulted. All operations are to be avoided. In suspected cases full examination of the blood must be carried out before any operation. Even a normal clotting and bleeding time and normal platelets do not always save the surgeon from disaster.

(5) *Osler's disease* is rare but embarrassing; bleeding occurs spontaneously from the skin and mucous membranes; several members of the family are similarly afflicted. The following case gives a typical picture: A man aged 40 gave a long history of severe epistaxis. This occurred daily for three weeks, resisting all accepted treatment, but the resulting anæmia may have caused cessation of the bleeding. On recovery from anæmia bleeding again started; this cycle had recurred over a period of years. Since cauterization had failed it was decided to use surgical diathermy under an anæsthetic; bleeding was extremely difficult to stop and there was no lasting effect. His father, an uncle, brother and a sister suffered from epistaxis.

(6) *Agranulocytosis*, as its name indicates, is a blood disease in which there is absence or great diminution of the granular cells in the blood. It occurs after the ingestion or injection of certain drugs—pyramidon, sulphanilamides (though not till 30 g. have been taken), sanocrysin, arsenical compounds and benzol. It is seen also after exposure to deep X-rays. Owing to the inflammation and ulceration of the tonsils, palate and gums the disease is called agranulocytotic angina. The disease has a high mortality. The patient is very ill with a high temperature often out of proportion to the condition of the pharyngeal lesions; death may take place in a few days. There is too, a chronic form in which treatment leads to temporary improvement in the blood picture; cases have lived for two years or more. Even slight operations are apt to produce serious relapses with extensive ulceration in the mouth; in one case extensive ulceration of the palate, gums and tonsil followed extraction of a tooth. Alcohol increases the symptoms; in some cases symptoms are connected with menstruation; a case has been seen as a complication of enteric fever. Rigors produced in the course of the disease lead to an enormous leucocytosis with cure. In a case recently published by Cross a leucocytosis of 40,000 followed a third blood transfusion for agranulocytosis and cure was immediate and permanent. One case of pemphigus has been seen in which prontosil caused disappearance of the skin lesions but was followed by agranulocytosis and on withdrawal of the prontosil the pemphigus recurred with fatal results.

(7) *Leukæmia* produces severe ulceration of the tonsil and is only distinguished from agranulocytosis and other tonsil ulcerations by a blood examination. Prognosis is fatal.

(8) *Achlorhydric anæmia.*—Professor Witts wrote an admirable paper on this subject analysing 50 cases; the symptom of dysphagia was one of the least frequent exhibited. The disease is a fruitful cause of chronic invalidism in women; its age-incidence is 30 to 50 (compared with 45 to 60 in Addison's anæmia). Most of the cases occur in the asthenic type of woman, her hair prematurely grey contrasting with dark eyebrows; the skin is pigmented but not icteric; anæmia is not obvious till a blood-count is done; the patients are often nervous and difficult; some have never felt well since girlhood, others date the onset from influenza or pregnancy. In 44 of the 50 cases achlorhydria was complete while in the remaining 6 faint traces only of free acid were present. Treatment consists in giving large doses of iron (iron and ammonium citrate) up to 240 grains a day, and is successful but return of hydrochloric acid in the gastric juice is never seen. The tongue may be bald towards the tip and dorsum. The dysphagia was only slight and transient in 4 cases, severe and the dominant symptom in 2. In my experience complete removal of the teeth has been carried out in almost all cases.

In 1919 Brown-Kelly described a symptom-complex in women complaining of dysphagia: spasm at the entrance to the œsophagus; smooth tongue; fissures at the corners of the mouth and pale pharyngeal mucous membrane. Œsophagoscopy showed a small circular lumen which could be opened easily with much relief. Similarly Paterson described a clinical type of dysphagia with spasmodic dysphagia and/or superficial glossitis; he noted also changes in the mucous membrane which tended to make it crack on the passage of a tube. The narrow lumen just below the cricoid appeared to be due to spasm of the crico-pharyngeus muscle and this led to the suggestion that this muscle was unable to relax.

There seems to be some tendency towards the development of malignant disease at the site of the narrowed lumen or perhaps on the posterior wall of the cricoid. Authorities are by no means in agreement about the frequency of this complication. Some speak of it as frequent but Vinson and Lamb consider it rare, and I incline to this view.

(9) *Avitaminosis* supplies two diseases with nose and throat manifestations—scurvy and rickets. Scurvy occurs usually between the ages of 6 months and 3 years; it causes hæmorrhages under the periosteum. When the swelling occurred over the frontal bone a mistaken diagnosis was made of acute osteomyelitis; incision revealed no pus and some lemon juice cured the patient. Laryngismus stridulus is a manifestation of rickets and may be confused with other causes of stridor.

(10) *Glandular fever* is characterized by sore throat and enlarged glands, at first cervical but later epitrochlear, axillary, inguinal and mediastinal; it is the last group that produces cough and perhaps stridor. The blood shows a leucocytosis up to 60,000 of which 80% are lymphocytes.

R. G. Macfarlane: I have subdivided the buccal manifestations of the blood disorders morphologically into hæmorrhagic, infiltrative, atrophic and ulcerative.

The hæmorrhagic lesions are usually manifestations of one or other of the hæmorrhagic states, associated with a vascular defect, or with faulty blood coagulation. In the hæmorrhagic purpuras there is usually a demonstrable vascular defect, revealed by decreased capillary resistance or a prolonged bleeding time which is often, but not always, accompanied by thrombocytopenia. These purpuras may be idiopathic, or secondary to toxæmia, aplastic anæmia, or leukæmia, and the type of bleeding they produce is characteristic. There is often persistent oozing from apparently intact mucous membranes, particularly of the nose and gums, which may in fact be the only symptom of the underlying disease. Bleeding into the tissues is in the form of petechial hæmorrhages or superficial ecchymoses, and deep hæmorrhages are rare. Hæmorrhagic telangiectasia is an example of a localized vascular defect. Lesions in the nose may produce such persistent epistaxis that a severe anæmia develops, but in the mouth they do not often bleed unless injured.

The other type of hæmorrhagic diathesis is due to defective blood coagulation, and includes hæmophilia and hypoprothrombinæmia. In these states uncontrollable bleeding as a rule follows injury and there is a liability to form extensive hæmatomata. I have seen a hæmophilic boy die of asphyxia following hæmorrhage into the base of the tongue before anything could be done to save him, and another who on several occasions developed hæmorrhage into the tissues of the throat, and required intubation, to prevent the impending asphyxia.

Infiltrative lesions are the result of deposition or proliferation of abnormal cells. In the leucoses, the cell type affected may infiltrate the mucous membranes of any part of the nose, throat, mouth or larynx. This infiltration may be diffuse or localized. Ulceration of the surface follows such invasion of the mucous membranes, usually in the acute leucoses, and particularly in the monocytic type in which angina and gingivitis may be the presenting signs. The lesions are complicated by the hæmorrhagic purpura that is frequently the terminal event in these diseases. There is no clearly defined boundary between the leucoses and frankly malignant states with a leukæmic blood picture. Leukæmic plasmocytoma may arise from any of the bones of the skull; leucosarcoma, involving the tonsils may have a leukæmic blood picture; and chloroma, with the blood picture of myeloblastic leukæmia, may invade any part of the skull and upper respiratory tract.

The origin of the mouth and throat lesions of glandular fever is more obscure, as autopsy material is rare. They are probably due to infiltration by the abnormal cells present in the blood, and Glanzmann (1930) considered that lymphocytic infiltration of the mucous membranes in some of his cases are responsible for them. Throat lesions occur in about 80% of cases and angina is not uncommon. The throat lesions of acute leukæmia, agranulocytosis, glandular fever and acute infection may be very similar. Examination

of the blood, or, if necessary, of the bone-marrow, will usually provide a certain differentiation.

The atrophic lesions include the glossitis, stomatitis, and pharyngitis that are associated with the deficiency anæmias, in which there is typically an atrophy of the surface epithelium; sometimes of underlying muscle accompanied by chronic inflammation and occasionally ulceration. There are many points of similarity between pellagra, sprue, steatorrhœa, pernicious anæmia, the tropical macrocytic anæmias, and the anæmia associated with gastro-intestinal operations and diseases. In all these there is a tendency to develop glossitis, stomatitis, and disorders of the gastro-intestinal tract, changes in the nervous system, pigmentation and lesions of the skin, anæmia, usually macrocytic, leucopenia and thrombocytopenia. Moreover all these conditions have been reported to respond favourably to treatment with crude liver, and their manifestations may be produced experimentally by withholding the factors contained in autolysed yeast known collectively as vitamin B. While pernicious anæmia will respond to a highly purified liver extract, the other conditions often fail to do so, though responding to crude liver or autolysed yeast.

It may be supposed, therefore, that these diseases are the result of a deficiency of the factors contained in crude liver, and derived from autolysed yeast, of which at least one, the anti-pernicious anæmia factor, requires the collaboration of Castle's intrinsic factor for its synthesis.

In pernicious anæmia the deficiency is conditioned by the absence of the intrinsic factor, and may be limited to the anti-pernicious anæmia factor as represented for the moment by anahæmin. The failure of other conditions to respond to anahæmin shows that these manifestations result from the lack of some other, or more than one factor.

The group of factors required probably includes nicotinic acid, riboflavine, the so-called extrinsic factor and others as yet unidentified. The lesions produced by their deficiency are almost certainly the result of the lack of these substances in the enzyme systems on which the living cell depends for its metabolism. The oxidation reduction processes, from which the energy for vital activity and growth is derived, are the result of such enzyme chain reactions. The first link of this chain is dehydrogenase, specific for each particular substrate, followed by co-enzymes 1 and 2, flavine enzyme and cytochrome. The co-enzymes contain nicotinic acid, flavine enzyme contains riboflavine, and cytochrome contains iron. The absence of any one of the links of this chain would bring the whole vital process to a standstill, and the partial deficiency of any one is likely to impair functional activity and growth.

If such a deficiency exists, evidence of it might be expected in those parts of the body where there is normally great activity, particularly in the production of new cells. The most obvious example of such tissue is the bone-marrow. Here there is a continual production of relatively enormous numbers of cells, roughly 50 g. of red cells and leucocytes, and an unknown quantity of platelets, every day. Deficiency of one or more of the factors required for growth and maturation results in a partial or complete breakdown in the process of production with consequent anæmia or leucopenia. Bone-marrow studies in the nutritional macrocytic anæmias reveal a very characteristic picture, that of arrested maturation. The marrow is full of primitive cells, most of which seem unable to develop beyond a certain point. The process of maturation when it does occur is distorted, resulting in the production of abnormal red cells and leucocytes. The disorder affects the red cell, white cell, and platelet precursors equally and in the peripheral blood the leucopenia and thrombocytopenia are usually as pronounced as the anæmia. If cells so dissimilar are all affected by lack of one or more of the maturation factors it is probable that other types of cell undergoing rapid production and maturation will be affected also. Witts (1932) has already compared the development of the cells of the bone-marrow to the development of the cells of the skin. Undoubtedly the skin and mucous membranes must provide a continual supply of new cells to replace those lost from the surface. Atrophic skin changes occur in the diseases we are considering, being most pronounced in pellagra, and least in pernicious anæmia, but the skin, being protected by its horny layer, is less susceptible to injury than the mucous membranes.

The epithelium of the mouth has probably to contend with more injury, chronic irritation, gross infection, violent changes in temperature and the application of noxious substances than any other part of the body. It would not be surprising therefore that any retardation of the continual production and maturation of new cells were followed by soreness, atrophy, or even ulceration. The changes found in the deficiency anæmias may be reasonably explained on this basis of general arrest of maturation. That each of the manifestations may occur separately, and will respond to treatment with crude liver suggests that each is the direct result of deficiency and that they are not inter-dependent. Whether it is the skin, gastro-intestinal tract, bone-marrow or nervous

system that is mainly affected depends probably on variations in diet, absorptive and digestive efficiency, and the requirements of the tissues concerned.

Iron deficiency may be accompanied by more specific changes resulting in a reduction of the hæmoglobin content of the red cell, and disordered development of the nails, both of which can be corrected by treatment with iron. Iron is also a factor in general metabolism, as it has already been shown that it is a constituent of cytochrome. The glossitis, atrophy of the lingual papillæ and pharyngitis may all be manifestations of this particular deficiency. The dysphagia that completes the Paterson-Kelly syndrome occurs in about 15% of iron deficiency anæmias. It has been reported in a few cases of pernicious anæmia, and is of importance because the atrophic changes and chronic irritation may predispose to carcinoma, particularly of the post-cricoid area.

Ulcerative lesions of the mouth and throat may be merely an exaggeration of the atrophic changes just described. I have recently been able to observe a case of nutritional anæmia with acute ulceration of the mouth, leading to perforation of the lower lip. The patient was a girl aged 14 years, with a previous history of cœliac disease. On admission she was desperately ill, with fever, and severe ulceration of the mouth. There was profound anæmia, the red cells numbering 1·6 million per c.mm., hæmoglobin 26% and only 600 neutrophils per c.mm. The platelets were 50,000 per c.mm. Bone-marrow examination showed a cellular marrow, with almost complete arrest of erythrogenetic and leucogenetic elements. The primitive red cells were definitely megaloblastic, and the whole picture resembled that found in pernicious anæmia. She was transfused and given liver and marmite, and in seven days the neutrophils rose to over 5,000 per c.mm., the platelets to 300,000 per c.mm., and the ulcers, one of which had perforated, were beginning to heal. She left hospital perfectly well in a month. A second case very similar to this was seen shortly afterwards, this time in a woman of 32 who had suffered from rickets and chronic diarrhœa. The ulceration was not so severe, but again there was an extreme degree of anæmia and leucopenia, and a megaloblastic hypercellular marrow; a rapid improvement followed blood transfusion and a course of liver and marmite. A similar condition has been described by Bowen-Davies (1934).

These cases introduce the problem of agranulocytosis, and the question whether the mouth lesions were due primarily to the maturation factor deficiency, or to the absence of granulocytes. Undoubtedly the granulocytes play an important part in limiting the spread of infection, once a break in the surface has occurred. Agranulocytosis superimposed on the atrophic stomatitis of the deficiency anæmias might be expected to result in severe angina. The granulocytes may be greatly reduced, however, without the occurrence of angina. I have seen cases in which neutrophils numbered 100 per c.mm. or less as a result of aplastic anæmia, X-ray irradiation and Felty's syndrome, without mouth lesions. Yet in toxic agranulocytosis there may be acute angina with 2,000 or more granulocytes per c.mm. (Plum, 1937).

Many cases of toxic agranulocytosis have followed the use of amidopyrine and related compounds, including the sulphanilamide derivatives. These drugs may produce in sensitive persons arrest of maturation or even disappearance of the granulocyte precursors in the bone-marrow. The red cells are usually stated to be unaffected, but in my experience, fatal cases following the use of sulphanilamide developed a profound anæmia and thrombocytopenia before death.

The possible mechanism of the toxic action of sulphanilamide in this respect might be considered more closely, because the effects of the drug on living cells have been carefully studied. Sulphanilamide not only inhibits the growth of leucocytes in certain people, it inhibits the growth of certain bacteria. Investigation of the latter action has shown that sulphanilamide blocks the metabolic process of the organism by interfering with a growth factor identified as para-aminobenzoic acid. This latter substance has a very similar structure to the sulphanilamide, and it has been suggested that the inactive sulphanilamide is incorporated, in mistake, so to speak, for the similar, but active para-aminobenzoic acid in an essential enzyme chain reaction that is thus brought to a standstill. The action can be inhibited by excess of para-aminobenzoic acid.

Dr. R. H. Mole has pointed out that sulphanilamide may have a similar action on developing leucocytes, and has suggested the use of para-aminobenzoic acid in the treatment of agranulocytosis. There is some evidence to favour the view that some at least of the toxic effects of sulphanilamide may be due to interference with the enzyme systems in which the vitamin B factors are concerned. Thus abnormal excretion of porphyrins occurs both in pellagra and following the use of sulphanilamide. Sulphanilamide produces a neuritis in animals that may be prevented by giving vitamin B, and it also produces skin lesions that may resemble those of pellagra. Vitamin B deficiency has already been shown to produce leucopenia and stomatitis, and it is possible that toxic agranulocytosis following sulphanilamide may be an extreme form of the same process. If this be so, therapy should be directed towards the supply of the deficient factor.

REFERENCES

BOWEN-DAVIES, A. (1934), *Guy's Hosp. Rep.*, **84**, 57.
GLANZMANN, E. (1930), "Das Lymphæmoide Drüsenfieber". Berlin.
PLUM, P. (1937), "Clinical and Experimental Investigations in Agranulocytosis". London.
WITTS, L. J. (1932), *Lancet* (i), **495, 549, 601** and **653**.

The President said that hæmophilia was probably the commonest blood disease encountered in routine work. Hæmophilia seemed to vary; at one period there might be very little bleeding, and at another time the patient was very susceptible. He had a child patient whom he knew to be a hæmophiliac and who had otorrhœa following measles and all the classical signs of an acute mastoid. He resolved, with a little misgiving, to operate. About three-quarters of an hour before operation a hypodermic injection of atropine was given. When the child was ready for operation he was still bleeding from the needle puncture, and therefore the operation was not done. The mastoid cleared up and the child recovered, but died later from hæmophilia.

Another type of case was acute leukæmia. During his long experience at the Royal Dental Hospital he had seen perhaps three of these cases. Attention was drawn to them by reason of a septic condition of the mouth and gums. Teeth were extracted, but bleeding continued, and the patient was admitted to hospital very ill, with a temperature of 104° or 105°, and ultimately died in about five days of septicæmia. Blood examination proved these to be cases of acute leukæmia.

Another condition which was seen frequently was an ulceration in the mouth or on the tonsil of which the diagnosis was uncertain. The Wassermann reaction was negative. It might be an agranulocytosis or some other obscure blood condition. Some cases of acute tuberculosis which were doing badly, with a painful superficial ulceration of the pharynx, epiglottis and larynx, might be mistaken for agranulocytic angina. It would be very easy to confuse a case of acute tuberculous ulceration of the pharynx with one of agranulocytosis. The white cell count in some cases of pulmonary tuberculosis was very low.

R. L. Flett said that caution was necessary when removing tonsils and adenoids in children with lymphatic leukæmia. In one case for removal of enlarged tonsils and glands in the neck in which he himself was not actually concerned the child died on the table and was found post mortem to have lymphatic leukæmia. In certain cases of leukæmia he had seen numerous ulcers down the pharynx and on the epiglottis, and there was some blood staining around each ulcer. He had also seen a Hodgkin's deposit on a vocal cord.

With regard to secondary anæmias where it was necessary to dilate the upper end of the œsophagus, he thought they did the cases some good, but a large number of those with atrophic mucous membrane began to form carcinomas afterwards. Recently he had dilated one of these strictures, secured a very good dilatation, and got the œsophagoscope to go past the stenosed area. A fortnight later he was called to see this patient because she was unable to swallow and was very ill. He thought he must have produced mediastinitis from his over-extensive dilatation, but when the patient died about a fortnight afterwards, a carcinoma was found about 3 in. from the cardia. The stenosed area was shown to be a healing area with a diamond-shaped space where it had been broken.

R. G. Macbeth, in expressing his appreciation of the papers, said that it was interesting to learn that avitaminosis perhaps took such an important part in blood diseases. Had Dr. Macfarlane noticed any increased tendency to bleeding from minor operations, such as tonsils and adenoids or removal of teeth, also had they noticed more cases of epistaxis associated with lowered vitamin intake? He thought he had been having more trouble during the last twelve months from reactionary hæmorrhage, and the dental surgeons said that they were encountering the same difficulty.

They were all accustomed to meet cases of, what he called, "normal abnormalities" such as the child admitted for tonsils and adenoids whose mother would say that, "of course, he always bled excessively if he cut his finger"; but in the majority of these cases there was an entirely normal bleeding time and clotting time. Occasionally these cases seemed to lose rather more blood at operation, but it was a clinical matter and could not be ascertained in absolute terms.

The question of female bleeders, otherwise healthy, also suggested itself. They were told that hæmophilia was transmitted on the female side but not inherited by the female. One occasionally found women who bled a good deal, and the nursing staff at his hospital were convinced that red-haired women always bled, and the anæsthetists sometimes gave their authority to the same story. A final question was: Should tonsil operations be avoided during the menstrual period?

J. F. Simpson said that it was quite true that one of his colleagues at a Royal Air Force hospital was disturbed during a short period by an unusual number of tonsillar hæmorrhages. He carried out a series of investigations on the vitamin content of the blood and put a number of the patients on to ascorbic acid treatment. The investigations did not show anything conclusive.

I. G. Robin said that recently a man aged 60, who had been treated at many hospitals for epistaxis from telangiectases, came in very ill with hæmoglobin under 25%. He had gradually improved on big doses of iron, vitamin K and nasal ionization and liquid paraffin drops. The mucous membrane of the nose was very dry and he bled from many points in the nose. The speaker was not sure how long he should go on ionizing; he was sceptical of the true value of the vitamin therapy.

Recently he diagnosed the Paterson-Kelly syndrome in a woman aged 50 who had had attacks of dysphagia several times and had been admitted to another hospital on a previous occasion. Before doing œsophagoscopy he got a physician to see her and he diagnosed pellagra; the condition cleared up completely on vitamin B. She had a low hydrochloric acid stomach content but no skin changes. The only changes were in the mouth, a very atrophic tongue and marked dysphagia.

J. C. Hogg said that there was a condition known as reticulosis which was characterized by ulceration in the upper air passages. It was apparently a disease of the reticulo-endothelial system, but perhaps Dr. Macfarlane could tell them whether it was, strictly speaking, a blood disease or not. The first case of the kind in his experience had Vincent's organism and looked like a typical Vincent's infection of the tonsils, though every investigation proved negative. His blood was examined by different pathologists, biopsies were taken of glands in the neck, but all were negative, and only when the patient died six months afterwards was the diagnosis established. He had ulceration of his larynx, pharynx, œsophagus, and intestines, and he believed of his stomach as well. Such cases were rare, but he had lately seen a similar case.

The President asked whether it was true that in cases of hæmophilia the clotting time was normal. The family history was very important.

Mr. Robin's case resembled multiple telangiectases of the septum. In one or two cases he had found a 5% solution of quinine and urethane injected between the cartilage and the mucoperiosteum prove successful.

This treatment was recorded by G. H. O'Kane (*J.A.M.A.*, 1938, 111, 242).

R. G. Macfarlane, in reply, said that in glandular fever sometimes the hæmatologist could not help very much in the diagnosis. The Paul-Bunnell reaction might be negative in 30 to 40% of cases and in these diagnosis could only be made on the abnormal type of lymphocyte occurring in the blood, which might not be present in very large numbers.

Several speakers had raised the question of the diagnosis of hæmophilia. In true hæmophilia he would have said the diagnosis was comparatively easy, because in almost all cases (about 98%) over the age of 5 or 6 years hæmorrhage into the joints occurred and was a characteristic feature of the condition. There was considerable variation in severity from time to time, there might be a normal coagulation time by the ordinary technique, but it was most important that the investigation be done with extreme care. If venipuncture were bungled there might be a normal coagulation time in hæmophilia, whereas if it had been done properly, the time would be four or five times the normal.

True hæmophilia, he believed, never occurred in females, but there was undoubtedly a hæmorrhagic tendency in some of the females through whom hæmophilia was inherited. He had seen one case of pseudo-hæmophilia in a woman in the sense that he could make no distinction between the condition in her case and that of true hæmophilia, but this was very rare indeed.

Unfortunately the tendency to bleed was not limited to the typical hæmophiliac. There were undoubtedly people who bled idiopathically, people in whom it was not possible to demonstrate any change whatever in the hæmostatic mechanism, but who were liable to bleed after operation or injury. In one woman who bled for six weeks after a small cut of the finger it was not possible to demonstrate any change in the hæmostatic mechanism.

Menstruation might be regarded as a hæmorrhagic diathesis. At the menstrual period there was a depression in the number of platelets and sometimes a prolongation of bleeding time, and although it was of no practical significance in the general run of cases it might be advisable to avoid the menstrual period for operation if possible.

Reticulosis was a collective term covering a large number of conditions, including Hodgkin's disease, so-called "atypical Hodgkin's disease", the leukæmias, the chloro-leukæmias, and the leuko-sarcomas, all of which might have a leukæmic blood picture. Reticulosis might not always have a typical blood picture. Hæmatologists could not as a rule diagnose reticulosis unless there were characteristic cells in the blood-stream.

Section of Therapeutics and Pharmacology

President—R. D. LAWRENCE, M.D.

[*February* 10, 1942]

DISCUSSION ON VITAMINS AND HÆMORRHAGIC STATES

Dr. Harold Scarborough: The literature dealing with the relation of the various vitamins to the different parts of the hæmostasis mechanism of the body is confusing, not to say contradictory. This unsatisfactory state of affairs is due to the injudicious selection of experimental material and to infrequent examination of the material selected. In order that future results shall be acceptable the following point should constantly be in the minds of those investigating these difficult and important problems: that "chronic" rather than "acute" forms of disorder be selected for investigation; and that "idiopathic" and not "symptomatic" cases be studied; that cases should be under close observation for at least fourteen days (preferably longer) before the effect of any therapeutic procedure is examined; and that all cases should give a history of excessive or abnormal bleeding extending over at least eight weeks, preferably longer; that female cases be excluded; and that observations should be made frequently since alterations of the various functions investigated sometimes occur with great rapidity and may be temporary.

The number of cases in any one centre suitable for investigation by these criteria is not large and my suggestion, therefore, is that comparatively little is likely to be achieved except by concentrated and, especially, co-ordinated attack.

Vitamin D.—The first known report of fatal bleeding in association with jaundice was apparently made by Wedels in 1683, since when it has been increasingly recognized that a proportion of jaundiced patients exhibit a latent hæmorrhagic tendency, which is liable to become manifest especially after operation. The observations on the relation of vitamin D to this condition which were originally made by Ivy and his associates (1935), and which have been confirmed by Boys (1937) and also by Johnston (1937) stand in danger of being swept away in the spate of literature on vitamin K.

Ivy developed a new technique for the determination of the bleeding time, the essential point of which is that a venous occlusion of 40 mm.Hg is applied through the cuff of a sphygmomanometer before the test is made. This manœuvre has certain consequences, viz. it may cause the bleeding time to be prolonged when the more usual technique (Duke) gives normal values, and, as a result, it becomes possible to demonstrate that vitamin D can reduce the bleeding time in patients with jaundice and certain other conditions. It is plain that a number of things may happen following the venous occlusion. One can imagine, for example, the increased intracapillary pressure exerting a greater tension on any clots that may be formed in the ruptured capillaries, a tension sufficient, if the clots be abnormally fragile, to force them from the capillaries and so prolong the bleeding time. On this basis vitamin D might be supposed to influence directly, or indirectly, the mechanism of clot formation. However, this explanation, which is evidently favoured by Ivy himself, raises the whole problem of the relative importance of the various factors taking part in the arrest of hæmorrhage from a small injury—a problem which itself awaits a complete answer.

One may recall in this connexion that Macfarlane (1941) has described structural and functional abnormalities in the capillaries in certain of the bleeding diseases, and I have frequently observed that venous occlusion may exert a profound effect on capillary resistance. There thus arises the attractive possibility that vitamin D may be concerned with the functional activity of the capillary walls.

Apart altogether from such considerations vitamin D is capable, in certain circumstances, of increasing the serum Ca, although the mechanism by which this increase is brought about and the fraction or fractions of the serum Ca which are so increased, are still undecided. A part of the serum Ca—and it is not at present clear which part—fulfils an indispensable function in blood coagulation and it may be on this basis that the phenomenon mentioned is to be explained. It is generally held that the non-diffusible Ca fraction consists of Ca bound to protein but it has been suggested (Watchorn and McCance, 1932) that it is to phospholipoid rather than to protein that the Ca is bound and there is experimental support for this view. Since there is evidence that vitamin D can alter the proportion of non-diffusible Ca in serum, then vitamin D might be supposed to influence the amount of Ca bound to phospholipoid. These points may then be considered in the light of the observations of Ferguson (1936, 1937) who believes that

thrombin is a "definite calcium-phospholipoid-prothrombin complex". On the experimental side it has been shown by a number of workers that irradiated ergosterol can shorten the clotting time in rats.

As in certain cases of jaundice, so in thrombocytopenic purpura, the bleeding time is usually prolonged. It is stimulating, therefore, in this connexion to recall the two cases of thrombocytopenic purpura reported by Lowenburg and Ginsburg (1936) to have been cured by means of a parathormone hypercalcæmia. A single similar case has also been reported by Levine and Michelson (1940).

Possibly these observations may be related to the fact reported on at least two occasions that the symptoms of parathyroid tetany are relieved by massive hæmorrhage, following which the serum Ca increases (Cruickshank, 1923, Swingle and Wenner, 1925). It is not at present clear how these various points are related.

Vitamin C.—Ascorbic acid immediately controls the hæmorrhagic manifestations of scurvy which, it may be noted, have been related to certain pathological changes in and around the smaller blood-vessels originally described by Wolbach and Howe (1926). Thrombocytopenic purpura is also characterized by a tendency to bleed and in this condition there is an associated capillary abnormality—a low capillary resistance. It seems not entirely unreasonable, therefore, by analogy to suppose that ascorbic acid might benefit this condition also. Vaughan, in 1937, came to the conclusion that the chances of favourably influencing the course of thrombocytopenic purpura by means of ascorbic acid was about 33%. Excluding the 21 cases referred to by Vaughan, we have been able to find 10 reports in the literature, 6 being unfavourable and 4 favourable. Further investigation would, therefore, seem to be justified. I have recently had the opportunity of treating 7 cases of thrombocytopenic purpura with massive doses of ascorbic acid without any demonstrable effect on the bleeding time, the thrombocyte count, or the capillary resistance.

It is widely held that a low capillary resistance is found in scurvy and that this is controlled by ascorbic acid. Determinations of the capillary resistance have been, and indeed are, used as a test for so-called sub-clinical scurvy. There is, however, an increasing body of evidence to suggest that the practice is unjustifiable. I have never found ascorbic acid to be capable of increasing capillary resistance except in very special circumstances. It is true that a low capillary resistance is frequently found in scurvy but it does not, therefore, follow that the lowness of capillary resistance is necessarily due to ascorbic acid lack. Scurvy, as met with to-day, is a complex deficiency state. It is also true, on the other hand, that the capillary resistance in scurvy may be found to be high. This is due to the fact that following the extravascular suffusion of blood into the tissues the capillary resistance becomes temporarily markedly increased (Scarborough, 1941*a*). Thus, if the test be performed shortly after bleeding into the tissues has occurred, a high capillary resistance will be found; if the capillary resistance be determined either before, or at some time after a hæmorrhage has developed, then a low result may be found.

Vitamin P.—The presence of this vitamin, whose very existence is still regarded by many as resting on the most tenuous evidence, was first announced by Szent-Györgyi and his associates (1936) as the result of observations on certain cases of purpura which were not benefited by administration of ascorbic acid. Although my observations require further independent support, I personally regard it as established that there is a substance or substances present in fruits, their juices and in certain extracts made therefrom which is capable in man of increasing the resistance of capillary walls to the application of pressure (Scarborough, 1939). The substance is not ascorbic acid but, so far as I know, no satisfactory proof exists that it is a flavanone although statements have been made to this effect. Animal experiments have as yet produced no collateral evidence though there is reason to suppose that this may be forthcoming shortly. In two subjects, by means of experimental feeding, evidence has been obtained that a clinical syndrome may be produced as a result of a specific deficiency of vitamin P in man. The major feature of this syndrome is petechial bleeding and an exhaustive hæmatological investigation of both cases at the time bleeding occurred revealed a remarkably low capillary resistance and a slightly prolonged bleeding time (Scarborough, 1940). These findings also require independent confirmation. It is well known, and I have repeatedly observed, that certain of the bleeding diseases are associated with a low capillary resistance. If it could be shown, therefore, that the development of purpura were dependent in whole or in part on an excessive fragility of the capillary walls, then the administration of a substance capable of controlling this function, viz. vitamin P, might be expected to be of value in their treatment. It has been found difficult to obtain convincing evidence on these points, but the following two cases are suggestive:

CASE I.—A female, aged 76, had for some years noted a tendency to bruise very easily and had for two years prior to her admission to hospital, been troubled with intermittent epistaxis. During the last nine months petechiæ had frequently appeared,

especially in the arms. There had been no previous or family history of hæmorrhagic disease and the dietary history was not significant. On examination the patient was a fairly well-nourished, healthy woman. Nothing abnormal was detected on examination of the cardiovascular system. The blood-pressure was 140/80. Renal function was satisfactory. Hæmatological examination revealed no cause for the hæmorrhagic tendency. The capillary resistance was found to be low.

A diagnosis of vascular purpura (purpura senilis) was made.

Fig. 1 (Case I) is a record of the capillary resistance of the patient determined in three separate areas of skin by a method I have already outlined (Scarborough, 1941*b*). The development of petechial bleeding is indicated at the bottom of the chart. The capillary resistance remained low during the preliminary period of twenty-six days, during which time a hæmorrhagic tendency was manifest. Administration of a preparation

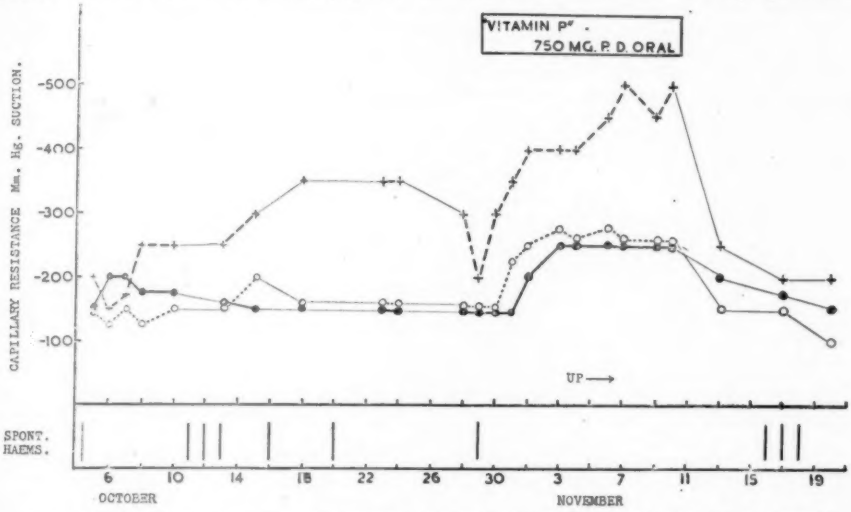


FIG. 1.—Chart of capillary resistance determined in terms of the least negative pressure (mm.Hg) required to produce a single petechia in each of three areas of skin. The development of spontaneous petechial bleeding is indicated below the chart by vertical lines. The effect of administration of a vitamin P preparation on capillary resistance and petechial bleeding is shown.

containing vitamin P coincided with an elevation of the capillary resistance and an absence of the manifest bleeding tendency in spite of the fact that the patient was allowed to get up during this period. With the cessation of vitamin P therapy the capillary resistance fell to its original level and the hæmorrhagic tendency returned.

CASE II.—A female, aged 65, for about ten years had complained of a marked tendency to bruising but of no other symptom. There were invariably one or more bruises on each arm and usually several on the legs. Ecchymoses could be readily induced by the "pinch" test. She had never complained of purpura but, on close examination on several occasions before the investigation began, petechiæ were noted in both upper and lower limbs. There was no previous or family history of bleeding and the dietary history appeared to be satisfactory. Nothing abnormal was detected during examination of the cardiovascular system. The blood-pressure was 135/64. Renal function was not impaired. Hæmatological examination revealed no cause for the bleeding tendency. The capillary resistance was low. A diagnosis of vascular purpura (purpura senilis) was made.

TABLE I.—CAPILLARY RESISTANCE. MM.HG. NEGATIVE PRESSURE.

	May	June	July	August	October	December
Area I	150	400	300	400	150	150
Area III	150	400	300	350	125	150
Area V	200	450	350	400	200	225

Bruising

Bruising

PERMIDIN 3 × 0·25 g.p.d. by mouth for 46 days.

PERMIDIN 3 × 0·25 g.p.d. by mouth for 29 days.

Table I (Case II) summarizes the progress of the case. Capillary resistance was initially low and associated with a tendency to bruise. A similar condition was again present at the end of the investigation which covered a period of seven months. During the periods indicated, a vitamin P preparation (Permidin) was administered. This apparently had the effect of increasing the capillary resistance and of controlling completely the bleeding tendency.

These two cases are merely suggestive and even when taken together certainly do not constitute proof of the value of vitamin P in the treatment of purpura. The present position is, I think, that vitamin P does exist but that it cannot at present be regarded as a potent therapeutic agent in any one of the bleeding diseases; indeed, I would go so far as to say that preparations of vitamin P should not be used for this purpose outside experimental centres. The clinical worker must await the labours of the chemist for the isolation or identification of the materials in fruit juices which possess capillary-resistance-increasing activity. It is, after all, illogical to make statements about the ineffectiveness, or otherwise, of vitamin P in the treatment of various forms of purpura until: (*a*) We know what vitamin P is; (*b*) we have preparations of it suitable for administration; and (*c*) we test their effect on selected cases.

REFERENCES

ARMENTANO, L., BENTSÁTH, A., BÉRES, T., ST. RUSZYNÁK, and SZENT-GYÖRGYI, A. (1936), *Deutsche med. Wchnschr.*, **62**, 1325.

BOYS, F. (1937), *Surgery*, **2**, 817.

CRUICKSHANK, E. W. H. (1923), *Biochem. J.*, **17**, 13.

FERGUSON, J. H. (1936), *Physiol. Rev.*, **16**, 640.

Id. (1937), *Am. J. Physiol.*, **119**, 755.

IVY, A. C., SHAPIRO, P. F., and MELNICK, P. (1935), *Surg. Gynec. & Obst.*, **60**, 781.

JOHNSTON, L. B. (1937), *J. Med.*, **18**, 235. Quoted in McCollum, E. V. (1939) "The Newer Knowledge of Nutrition". 5th Edition. New York.

LEVINE, D. B., and MICHELSON, H. (1940), *J. A. M. A.*, **115**, 360.

LOWENBURG, H., and GINSBURG, T. M. (1936), *ibid.*, **106**, 1779.

MACFARLANE, R. G. (1941), *Quart. J. Med.*, **33**, 1.

MCNEALY, R. W., SHAPIRO, P. F., and MELNICK, P. (1935), *Surg. Gynec. & Obst.*, **60**, 785.

SCARBOROUGH, H. (1939), *Biochem. J.*, **33**, 1400.

Id. (1940), *Lancet* (ii), 644.

Id. (1941*a*), *J. Physiol.*, **100**, 8P.

Id. (1941*b*), *Edinburgh M. J.*, **48**, 555.

SWINGLE, W. W., and WENNER, W. F. (1925), *Am. J. Physiol.*, **75**, 378.

VAUGHAN, J. M. (1937), *Brit. M. J.* (ii), 842.

WATCHORN, E., and MCCANCE, R. A. (1932), *Biochem. J.*, **26**, 54.

WEDELS, G. W. (1683), "De haemorrhagia universali". Lipsiae, 1670-1702, **2**, 318. Quoted from Butt, H. R., and Snell, A. M. (1941), "Vitamin K", Philadelphia.

WOLBACH, G. B., and HOWE, P. R. (1926), *Arch. Path.*, **1**, 1.

VITAMIN K, AND THE ESTIMATION OF PROTHROMBIN

Dr. R. G. Macfarlane: The discovery of vitamin K, and the recognition and treatment of conditions in which it is deficient, mark one of the greatest advances in the field of the hæmorrhagic states.

Several naturally occurring derivatives of 1; 4-naphthoquinone have vitamin K activity. Vitamin K_1 occurs in many plants and vegetables, particularly alfalfa, spinach and cabbage. A slightly less active analogue, vitamin K_2 occurs in putrefying fish meal presumably as a result of bacterial synthesis. The substance now known as vitamin K_3 was isolated in 1933 by Anderson and Newman from tubercle bacilli, though at that time they were unaware of its activity as a vitamin, and named it phthiocol.

Apart from these, some thirty synthetic compounds with similar activity have been reported. The majority are also derivatives of 1; 4-naphthoquinone, of which the 2 methyl-derivative known as vitamin K_3 is the most familiar. The activity of the various synthetic derivatives is greatly influenced by apparently minor alterations in structure.

Vitamin K deficiency in man may be due to deficient diet, absorption, or utilization. Simple dietary deficiency is rare, although a few probable instances have been reported (Kark and Lozner, 1939; Scarborough, 1940). Vitamin K is found in large amounts in the fæces, where it is probably derived from bacterial synthesis, and this intrinsic source may well reduce the incidence of clinical manifestations that might otherwise result from deficient intake. Hæmorrhagic disease of the newborn has been shown by many workers to respond to treatment with vitamin K, and it has been suggested that there is normally a deficiency of the vitamin during the first few days of life, conditioned by deficient intake and the absence of bacteria from the intestinal tract (Quick and Grossman, 1939). Such

a deficiency accentuated by other factors is probably responsible for the disease. Deficient absorption of the vitamin is a more frequent abnormality and may be due to absence of the bile salts following obstructive jaundice, or to intestinal defects resulting in general malabsorption, such as sprue, steatorrhœa, gastro-intestinal fistulæ, and short-circuiting operations. Deficient utilization is said to follow liver damage and to be unresponsive to treatment. It has even been suggested that the response to vitamin K is an index of liver-function as reliable as the excretion of hippuric acid (Wilson, 1939). Recent work, however, suggests that there is actually little correlation between liver damage, evidence of vitamin K deficiency and response to treatment (Lucia and Aggeler, 1941).

The result of extreme vitamin K deficiency in man and in animals is the development of a hæmorrhagic diathesis, which responds, except in some cases of liver damage, to adequate treatment with the vitamin. The type of bleeding that occurs is illustrated by hæmorrhagic jaundice, and hæmorrhagic disease of the newborn. There is a liability to bleed persistently from injuries, from the gastro-intestinal tract, or into the tissues. Coagulation of the blood is delayed, the bleeding time is sometimes prolonged in jaundice and almost invariably prolonged in hæmorrhagic disease of the newborn, the platelets and capillary resistance are apparently normal. It is now almost universally accepted that these manifestations are due to a reduction in the amount of plasma prothrombin, in turn dependent on the deficiency of vitamin K. While there can be no doubt that the coagulation of the blood is impaired in these conditions, it is difficult to explain all the manifestations on this basis alone. The prolonged bleeding time is an example. It has been repeatedly shown that the bleeding time is not influenced by coagulation of the blood and I maintain that it is an index of capillary contractility (Macfarlane, 1941). The same remarks apply to the " needle puncture hæmatomata " regarded by Kark and Souter (1941) as characteristic of hypoprothrombinæmia, and which do not occur in other conditions with defective coagulation, such as hæmophilia. Macpherson (1941) has shown that the prolonged bleeding time in hæmorrhagic disease of the newborn becomes normal following treatment with vitamin K, suggesting that a capillary defect may accompany the vitamin deficiency.

If the existence of a coagulation defect is established beyond doubt in these conditions, the nature of this defect is not quite so obvious, and it is necessary to examine the methods which claim to estimate prothrombin before the significance of their results can be assessed. These methods fall into two main groups, those using the single stage as introduced by Quick (1935) and modified by a large number of subsequent workers, and the two-stage methods. The latter as devised by Warner, Brinkhous and Smith (1934), and particularly the modification by Herbert (1940) avoid many of the fallacies of the single-stage group, but are so elaborate and introduce so many pitfalls of their own that they are not yet available for the ordinary laboratory practice.

Quick's test, or some modification, has been widely used in the detection of hypoprothrombinæmia, and the assay of human responses to vitamin therapy. The procedure depends upon the dogma that " in the presence of an excess of thromboplastin and a sufficient amount of calcium, the coagulation time of blood or plasma is proportional to the amount of prothrombin it contains ". Details of the remaining part of the procedure do not seem to matter so much. The test can be done on whole blood (Ziffren *et al.*, 1939), oxalated blood (Innes and Davidson, 1941), oxalated plasma (Quick, 1935). If recalcification is carried out it can be done with a fixed amount of calcium (Quick, 1935) or a variable optimum amount (Pohle and Stewart, 1939). The term thromboplastin has included rabbit brain, fresh, heated, dried or extracted with acetone; human brain (Owen and Toohey, 1941); dog, horse or ox lung, Russell's viper venom (Fullerton, 1940) or Russell's viper venom and lecithin (Hobson and Witts, 1941). The normal coagulation time by these different methods varies from about 7-35 secs. and it would be proportional to varying prothrombin concentration only if certain assumptions are correct. Some of these are as follows, beginning with the fibrin end of the clotting process:

(1) It is assumed that a given amount of thrombin will necessarily clot different samples of blood or plasma in the same time. This may not be the case. Thrombin is rapidly destroyed in normal blood and variations in this antithrombic activity will alter the coagulation time. Moreover, quite large differences in the reactivity of fibrinogen to thrombin have been observed (personal observation, Herbert, 1941) and variations in fibrinogen concentration may be large and will alter the speed of the reaction.

(2) It is assumed that the rate of thrombin production and hence the coagulation time depends only upon the concentration of prothrombin in the presence of excess of thromboplastin. This is not the case. The rate of production of thrombin depends also on the reactivity of the prothrombin to the particular thromboplastin used, on calcium and electrolyte concentration, pH, and many other factors often not controlled. The time relations between activation and coagulation are also involved. If we accept Warner,

Brinkhous and Smith's definition of a unit of thrombin as that amount which will clot 1 c.c. of standard fibrinogen solution in fifteen seconds, then normal plasma will produce about 300 units per c.c. Coagulation may occur within a few seconds of the production of a small fraction of the available thrombin, and further thrombin production goes on for several hours after coagulation is complete (Warner *et al.*, 1936). In other words, when Quick's test is all over, anything up to 95% of the prothrombin that was to be estimated remains unconverted. The practical importance of this relationship is that the test is sensitive to slight changes in reactivity of the prothrombin but relatively insensitive to changes in prothrombin concentration. This is illustrated by Quick's own curve (1938) which demonstrates little change in coagulation time between 100% and 40% prothrombin concentration.

(3) It is assumed that equal amounts of any one of the thromboplastic agents already mentioned will clot different samples of blood or plasma in the same time if the prothrombin concentrations are equal. This assumption leads us into very deep water, because so little is known about thromboplastin. The generally accepted view is that thromboplastin is a lipoid substance present in platelets and body tissues, and the older view that thromboplastin was an enzyme—the thrombokinase of Morawitz—has been discounted (Mertz *et al.*, 1939). It has seemed to me for some time, however, that both views might be correct, and that what is known as thromboplastin is in fact two separate substances, one being a water-soluble enzyme, and the other a lipoid substance that is either catalyst or substrate.

In support of this view there is the analogy of the action of Russell's viper venom. The venom is a water-soluble enzyme-like substance, which behaves as an extremely powerful thrombokinase. Trevan and I found that its action could be greatly accelerated by the addition of tissue suspensions, fat fractions, or by crude lecithin (1936). Moreover, we have been able to show that if plasma is defatted by spinning at 25,000 revolutions per minute or by extraction with solvents, Russell's viper venom is incapable of clotting it unless lecithin or tissue fat is added (Macfarlane, Trevan and Attwood, 1941). We have not been able to show as yet that substances analogous to the venom and lecithin are actually required for normal coagulation, but there is some indirect evidence in support of this view. For instance, saliva contains a thrombokinase-like coagulant, and since the venom is a modified saliva, it is not unreasonable to suppose that the action of one may be merely a greatly exaggerated form of the other. Defatted saliva, like venom will not clot defatted plasma until the fat fraction is supplied. A major difference is in the effect of lecithin which will actively potentiate venom but has no effect on ordinary coagulation. Lecithin has, however, occasionally brought about the coagulation of defatted plasma, suggesting that it can activate the normal enzyme in the absence of the normal lipoid.

The provisional hypothesis, therefore, is as follows. Fresh tissues contain a venom-like enzyme, and a lipoid factor. The two factors together constitute what is known as thromboplastin and each is inactive separately. Plasma also contains both factors, the enzyme being in relative excess. Ordinary coagulation is the result of the reaction between these two factors and prothrombin in the presence of calcium. The addition of tissue extracts accelerates the normal reaction, because it increases the concentration of available lipoid. Russell's viper venom and lecithin represent the addition of both factors and result in the most rapid coagulation yet observed.

If this view of thromboplastin is correct, it will be seen that, in the estimation of prothrombin, no attempt to keep the enzyme factor constant is made, except in the methods using venom. Venom alone is liable to give variable results as it is greatly affected by small variations in available lipoid as shown by Crosbie and Scarborough (1941). The addition of a relatively large constant amount of lecithin as used by Hobson and Witts should control this variable.

Whether this view of the composition of thromboplastin is correct or not the procedures in use in the single-stage method are open to many objections. No account is taken of varying antithromboplastic activity either in the blood under test or in the thromboplastin itself. What is probably more important is that no allowance can be made for variations in the individual reactivity between prothrombin and thromboplastin, nor of the species specificity which has been shown by Trevan (unpublished) to be an important factor in the speed of the reaction, and which may vary from one sample of plasma to another.

There are many other theoretical objections to the single-stage method, but what is more significant is that there are serious discrepancies between the results obtained by the probably more reliable two-stage method and those obtained by the single-stage method. For instance, the incidence of hypoprothrombinæmia in jaundice as determined by the two-stage method is nearly twice that as determined by Quick's method (Brink-

hous, 1940). By the two-stage method, dogs and men have approximately identical prothrombin values, but by the single-stage method man has only one-fifth of the normal dog value (Quick *et al.*, 1935; Warner *et al.*, 1939). In newborn babies, the two-stage method indicates that prothrombin is reduced to 14-40% of normal, but the single-stage method gives normal values (Brinkhous *et al.*, 1937; Quick and Grossman, 1939).

The most striking anomaly has been provided by the use of the substances responsible for hæmorrhagic sweet clover disease in animals, considered to be due to a prothrombin deficiency (Roderick, 1931; Quick, 1937). Link and his associates have discovered that the disease is the result of a toxic agent identified as 3; 3′-methylenebis (4-hydroxycoumarin). The effect of this substance on dogs was studied by Bingham and his co-workers (1941), who found that it produced in addition to hæmorrhagic manifestations, liver destruction and changes in the capillaries. The protocols of their observations on the blood reveal the extraordinary fact that whereas the ordinary blood coagulation time was only a few minutes, the so-called prothrombin times on corresponding samples by Quick's method was many hours (Bingham *et al.*, 1941, *see* Table I, p. 568). In other words, the thromboplastin added inhibited coagulation. Not the least remarkable point is that the authors themselves make no comment on this anomaly and apparently accept the delayed clotting times as an estimate of prothrombin.

Similar results have been obtained by Witts (1942) in the case of a man given the coumarin compound. Again there was inhibition of coagulation by dried rabbit brain since the "prothrombin time" was more than half an hour, as against four minutes if calcium alone were added. Fresh human brain slightly accelerates the clotting time, and if Russell's viper venom were added to the dried brain coagulation occurred in 13½ seconds. We were able to confirm these results.

It is quite clear that Quick's test has broken down completely where the coumarin compound is concerned. Any attempt to explain the results on the facts so far available would be pure speculation but I cannot resist the temptation. It may be that the inhibition by rabbit brain is an exaggeration of the species specificity, already mentioned. A more attractive but less probable explanation is that coumarin reduces the enzyme component of thromboplastin normally present in the plasma. While there remains enough to produce clotting in four minutes on the addition of calcium the addition of a great excess of lipoid in the form of dried brain results in inhibition, a phenomenon frequently seen in precipitin and agglutinin reactions if one of the reactants is in great excess. Fresh brain, because it contains some enzyme, does not inhibit the reaction so markedly. Venom and brain produce rapid coagulation, because the venom supplies the required enzyme.

I have tried to show that Quick's test as usually performed may measure prothrombin, but certainly measures many other variables as well. Russell's viper venom and lecithin seem to be a more reliable source of thromboplastin than the various animal tissues, variously treated, that are so widely used. If Quick's test is to be used at all, and it is a simple and in many cases a valuable procedure, it should no longer be called the "prothrombin time" but rather the "accelerated clotting test" as suggested by Professor Witts.

REFERENCES

ANDERSON, R. J., and NEWMAN, M. S. (1933), *J. Biol. Chem.*, **103**, 405.
BINGHAM, J. B., MEYER, O. O., and POHLE, F. J. (1941), *Am. J. M. Sc.*, **202**, 563.
BRINKHOUS, K. M. (1940), *Medicine*, **19**, 329.
BRINKHOUS, K. M., SMITH, M. P., and WARNER, E. D. (1937), *Am. J. M. Sc.*, **193**, 475.
CROSBIE, A., and SCARBOROUGH, M. (1941), *Brit. M. J.* (i), 268.
FULLERTON, M. W. (1940), *Lancet* (ii), 195.
HERBERT, F. R. (1940), *Biochem. J.*, **34**, 1554.
HOBSON, F. G. G., and WITTS, L. J. (1941), *J. Path. & Bact.*, **52**, 367.
INNES, J., and DAVIDSON, L. S. P. (1941), *Brit. M. J.* (i), 621.
KARK, R., and LOZNER, E. L. (1939), *Lancet* (ii), 1162.
KARK, R., and SOUTER, A. W. (1941), *Brit. M. J.* (ii), 190.
LUCIA, S. P., and AGGELER, P. M. (1941), *Am. J. M. Sc.*, **201**, 326.
MACFARLANE, R. G. (1941), *Quart. J. Med.*, **33**, 1.
MACFARLANE, R. G., TREVAN, J. W., and ATTWOOD, A. M. P. (1941), *J. Physiol.*, **99**, 7P.
MACPHERSON, A. I. S. (1941), *Brit. M. J.* (ii), 433.
MERTZ, E. T., SEEGERS, W. H., and SMITH, M. P. (1939), *Proc. Soc. Exper. Biol. & Med.*, **41**, 657.
OWEN, T. K., and TOOHEY, M. (1941), *Lancet* (i), 724.
POHLE, F. J., and STEWART, J. K. (1939), *Am. J. M. Sc.*, **198**, 622.

QUICK, A. J. (1935), *J. Biol. Chem.*, **109**, lxxiii.
Id. (1937), *Am. J. Physiol.*, **118**, 260.
Id. (1938), *J. A. M. A.*, **110**, 1658.
QUICK, A. J., STANLEY-BROWN, M., and BANCROFT, F. W. (1935), *Am. J. M. Sc.*, **190**, 501.
QUICK, A. J., and GROSSMAN, A. M. (1939), *Proc. Soc. Exper. Biol. & Med.*, **40**, 647.
RODERICK, L. M. (1931), *Am. J. Physiol.*, **96**, 413.
SCARBOROUGH, M. (1940), *Lancet* (i), 1080.
WARNER, E. D., BRINKHOUS, K. M., and SMITH, M. P. (1934), *Arch. Path.*, **18**, 587.
Id. (1936), *Am. J. Physiol.*, **114**, 667.
Id. (1939), *Proc. Soc. Exper. Biol. & Med.*, **40**, 197.
WILSON, S. J. (1939), *ibid.*, **41**, 559.
WITTS, L. J. (1942), *Glasgow M. J.* (in press).
ZIFFREN, S. E., OWEN, C. A., HOFFMAN, G. R., and SMITH, M. P. (1939), *Proc. Soc. Exper. Biol. & Med.*, **40**, 595.

Mr. A. L. Bacharach said that recent work had confirmed the claims of Zacho and of Ruszynák and Benko to have produced a lowered capillary resistance in guinea-pigs receiving a scorbutogenic diet together with large daily doses of pure ascorbic acid. This capillary fragility was prevented or reversed by the administration of certain concentrates from citrus fruits and other sources, including the black-currant and rose-hips. Highly purified hesperidin, one of Szent-Györgyi's original sources of vitamin P activity, was also active, though less so than a more soluble product made from citrus peel by a modification of Szent-Györgyi's published procedure for preparing "citrics". The results so far obtained had been made the basis of a quantitative biological assay method, and it was hoped that this would help towards elucidating the distribution and chemical nature of vitamin P, and so indirectly its physiological role and therapeutic use.

Section of Odontology

President—HAROLD ROUND, M.D.S.Birm., L.D.S.Eng.

[*January* 26, 1942]

Experiences with Various Methods of Skeletal Fixation in Fractures of the Jaws

By RAINSFORD MOWLEM, F.R.C.S.

IN order to find fifty instances of the use of some method of fixation which was not solely related to the teeth, it was necessary to review the records of only 120 consecutive cases of fractures of the mandible or maxillæ, which had been treated in the Plastic and Jaw Centre at an E.M.S. Hospital. This, then, is one excuse for the incursion of a surgeon into what might be regarded as a dental field. Another is the fact that as a member of the Repair Team, the surgeon is often dependent upon immediate primary replacement of facial fractures before he can undertake the repair of soft tissues. He is therefore concerned to use methods which are immediately applicable and which do not impose limitations on his activities. A further excuse is that the method of fixation of mandibular fragments which are to be the site of a bone graft, may affect the technique of the operation.

The multiplicity of the fractures in any given case may have some bearing on the method of treatment of each part, and it may determine the order in which this treatment should be applied. The nearest intact bone may well be the vault of the skull; the plane of the teeth must be rigidly anchored to this and once this is done a basis for support of, say, the orbital floor or the malar zygomatic compound is obtained. In such circumstances it seems obvious that efficiency can be obtained only by a Team consisting of a surgeon, a dental surgeon, and a mechanic. To these must be added an anæsthetist, upon whose skill the possibility of early treatment is often dependent. Each man must have a working knowledge of the technical problems confronting the other members of the Team. Under such a regime it is unlikely that any part of the repair will fail to receive its due share of attention. Soft tissues will not be sutured without adequate primary bone fixation. Dental occlusion will not be obtained whilst orbital disorganization is overlooked. Bone control will not necessarily be thought of only in terms of teeth.

The cases illustrated have been chosen partly because they are unorthodox, but mainly because they show how combinations of simple methods may often solve difficult problems. It is not to be assumed that any illustration is regarded as the correct method of treatment for any given fracture. Some of the methods we may never use again, and others may well be inapplicable to a case which is apparently identical with that illustrated.

WIRE

Wire has been used in dentistry for many years and there can be very little that is new in its application. One of its great advantages is that it is readily available and by a little ingenuity can be made to solve awkward problems, particularly when the services of a mechanic and his laboratory are not available. There appear to be occasions upon which its very simplicity may determine its use even in the best equipped unit. At the beginning of the war, soft brass ligature wire, 22-24 gauge, was chiefly used. Later we were able to obtain annealed stainless steel of the same gauge, and this is now preferred because it has less tendency to stretch.

MANDIBULAR APPLICATIONS

Circumferential wires have been used for many years. For the edentulous jaw they are often the only method of treatment. There appears to be some diversity of opinion about the difficulties associated with their use. The first difficulty is that of insertion. This is simplified by the use of a fine curved cannula, the bore of which will just accommodate the wire. There has also been some difference of opinion as to whether it is safe to insert the wire from within the mouth. We have always used this route because it is easier to

keep close to the bone, and thus avoid the inclusion of soft tissues in the bite of the wire. At the lower margin of the mandible there is a small triangle of tissue which cannot be avoided. This is always severed by sawing the wire backwards and forwards three or four times before twisting it into position over the splint. This obviates two difficulties; first, pain due to the inclusion of this tissue, and second, slackening of the wire which occurs when the included tissue gradually gives way under pressure. With regard to the question of infection when the oral route is used, we have experienced only one case in which it was necessary to drain a small abscess, and even this was at the site of a previous infection secondary to osteomyelitis. The X-rays shown in fig. 1 illustrate the ordinary type of metal trough splint tied into position over the mandible. In this case it was used to fix the mandible prior to the bone graft shown in the lower illustration. A useful elaboration is shown in fig. 2. In this case there was a fracture in the body of the mandible together with a fracture of the right condyle, and both the condyle and the coronoid process on the left. The posterior circumferential wires carried additional wire loops which emerged through the skin. These were then fixed to vertical rods and distraction of the condylar fractures so obtained.

Angle wires.—These have been almost completely discarded because of their failure to immobilize a posterior fragment. With traction to a headcap, the ordinary angle wire does control flexion at the temporo-mandibular joint, but does not correct adduction without increasing rotation. In addition the fragment still moves with swallowing.

MAXILLARY APPLICATIONS

Cheek wires.—When the maxilla is completely floating and perhaps especially when there is an antero-posterior palatal fracture with differences in level of the two sides, a simple method of suspension by wire appears to work well. A plaster skull-cap with horns over the outer halves of the supra-orbital ridges is applied.

(It may be justifiable to diverge here to say a word about these caps. Our own preference is for the completely unpadded type from which the hair is protected by a single layer of stockinette. There are two essential parts to the cap. The first is the horizontal band which carries the appliance. This must be carefully moulded well down below the occipital protuberance, and must not press on the supra-orbital ridges. The second part consists of a vertical band from the preauricular area on one side across the vertex to the opposite side. This should carry the weight, and no pressure beyond that necessary to obtain close apposition to the occiput should be exerted by the horizontal band. The posterior quadrant of the cap is left open, both for the sake of lightness and to allow the hair to escape. This will be seen in figs. 3, 4, 5 and 6.)

Cap splints are constructed for the upper and lower jaws. On the maxillary splint an inverted hook is provided in the region of the first premolars on each side. The jaws are closed together in correct occlusion, and it is obvious that for this purpose the mandible must be used as a guide. Elevation of both the maxilla and the mandible is obtained by passing a wire from the horns of the plaster skull-cap to the hook on the cap splint through the soft tissues of the cheek. Spring loading can be applied if necessary and by this means correct reposition obtained. Fig. 4 shows a wire on the left side, with elastic loading to elevate the maxilla. The right half of the bone was controlled by a tube threaded over the wire. This will be mentioned later.

The lower X-ray in fig. 1 shows the attachment of such wires to the cap splint.

It might be thought possible to raise the maxilla too high by such a method, but in our experience this is not the case.

A modification for use in the absence of facilities for the construction of cap splints has been tried in an extremely extensive fracture of the maxilla. Diplopia and cerebro-spinal rhinorrhœa were present. Arch wires were fixed to upper and lower teeth and correct occlusion obtained. The cheek wire was then passed downward, not to the maxillary but to the mandibular arch. This was to avoid any tendency to laceration of the gums. Immediate complete control was obtained and there have been no difficulties in spite of the fact that the patient was nursed by reason of other injuries under an ordinary surgical regime. The presence of the wire in the cheek occasions the patient no discomfort and subsequent scarring is rarely visible, if care is taken to insert the wire in a direct line from the cap to the splint.

Maxillary alveolar wiring was introduced in this country by our colleagues, Messrs. Kelsey Fry, McLeod and Walker, at East Grinstead. Briefly, it consists of actually tying a splint on to the superior maxilla by two or three wires passed through the alveolus. Care must be taken to avoid the antrum. There are one or two technical problems concerned with the insertion of the wire at a level which makes it possible to keep the splint tight, but these are not insuperable. Fig. 2 shows a case in which the upper splint was tied into position and the wires effecting this can be seen in the X-ray views.

FIG. 1.—The loss of right ascending ramus. Mouth edentulous. Fixation obtained by double metal trough splint, the upper half being suspended to a skull-cap and the lower half wired on to the mandible.

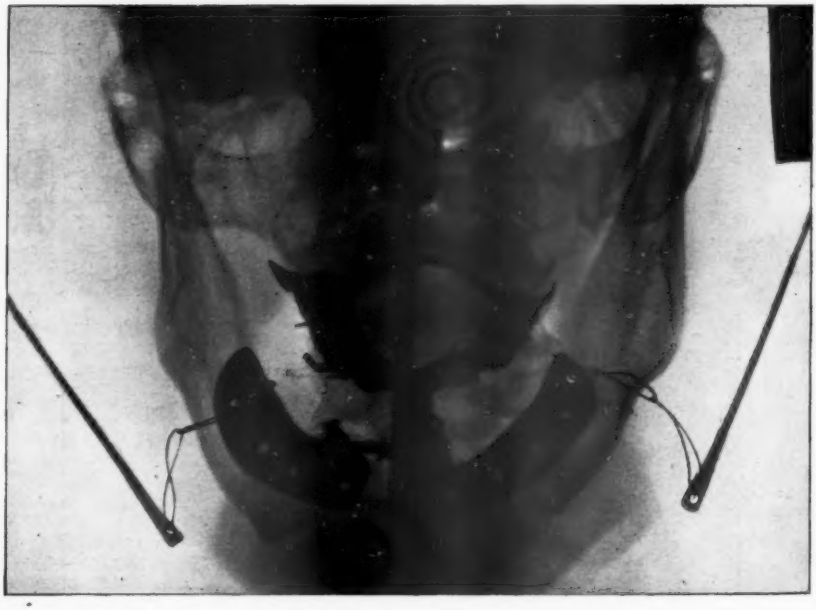


FIG. 2.—Fracture of right condyle, body of mandible, left condyle and left coronoid. Patient edentulous. Mandibular splint wired on, downward distraction at the angles, maxillary splint secured by alveolar wiring. The same patient is illustrated in fig. 3.

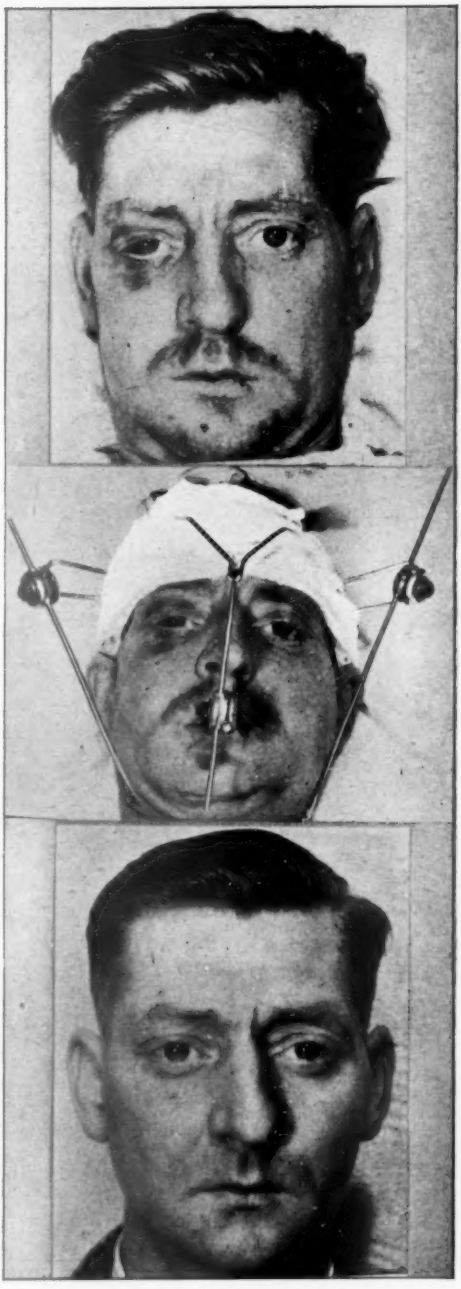
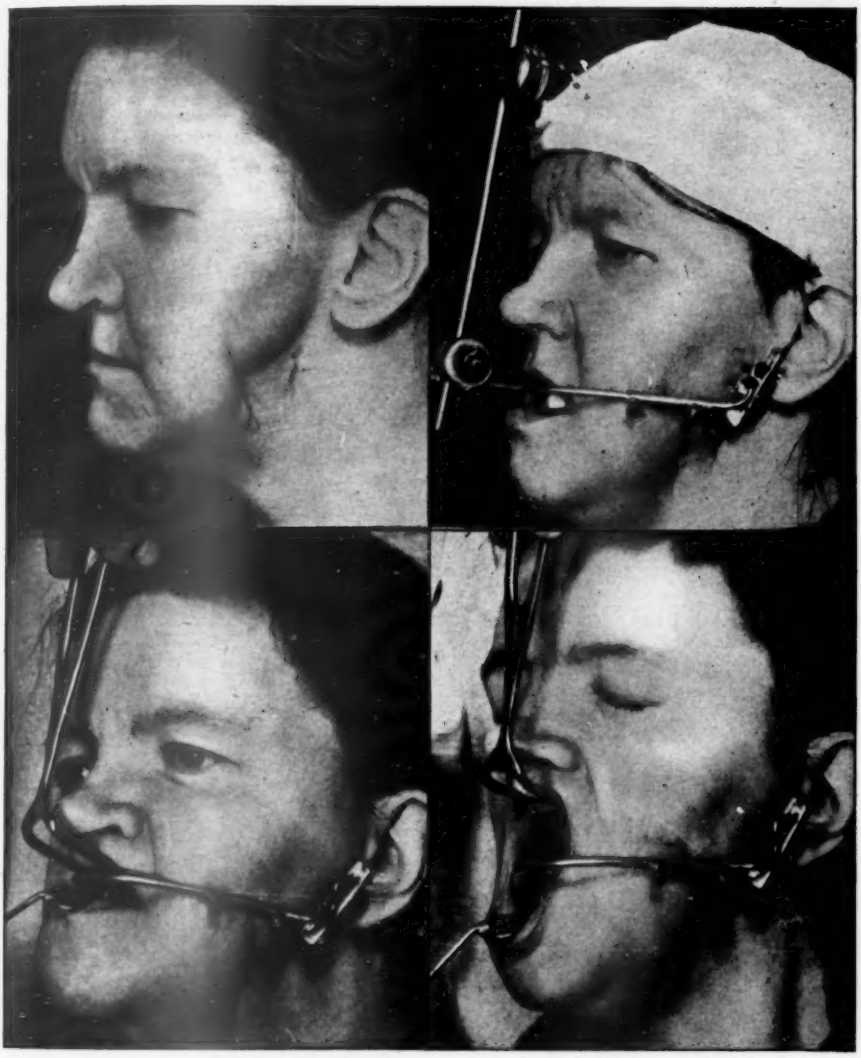


FIG. 3.—Views of pre-operative, operative and post-operative treatment of patient whose X-rays are shown in fig. 2.

FIG. 4.—Transverse fracture of superior maxilla with displacement backward and to the right, of three months' duration. Surgical mobilization followed by spring loaded traction on the left side, counter-pressure on the right side and forward traction by weight and pulley.

A B



C D

FIG. 5.—Bomb injury with bone loss. Marked flexion of posterior fragment shown at A. Pin fixation to sliding bar from lower trough splint, together with fixation to skull-cap shown at B. Degree of movement of mandible as a whole shown at C and D. X-rays of this patient shown in fig. 9.

FIG. 6.—Apparatus devised by Squadron Leader A. B. MacGregor, R.A.F.V.R., giving threaded screw control for the maxilla.

FIG. 7.—Typical application of the cross-pin method of fixation for fractures at or near the angle.

FIG. 8.—Fracture at the angle with medial displacement, rotation and flexion of the posterior fragment, shown at A, appliance in position shown at B and result at C.

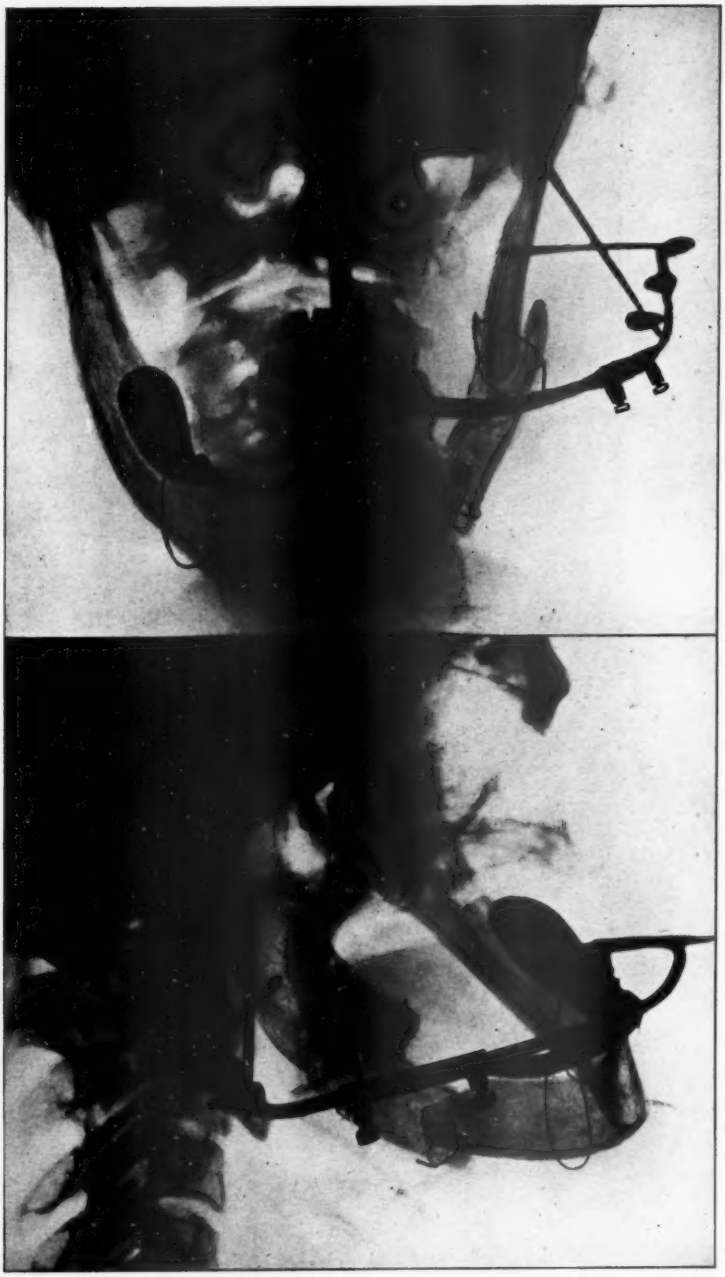


FIG. 9.—X-ray of patient illustrated in fig. 5. Lower metal trough splint wired on to mandible, bar emerging from mouth to connect with pins in the posterior fragment. Bone graft is shown in position. The appliance shown in view A corresponds with 5B, view B with 5D.

Rod and Bar Fixation

This is a well-tried method, though some of its applications may be relatively new. We have abandoned the Kingsley type of splint because of its inaccuracy and instability. Its place has largely been taken by direct rod fixation from the plaster cap; the use of small universal joints has simplified this technique enormously and fig. 5 illustrates a typical vertical bar with two universal joints. One-eighth inch silver steel or German silver rod is most commonly employed.

The horizontal part of the appliance in fig. 5 is described later.

MANDIBULAR APPLICATIONS

Control of the edentulous posterior fragment.—Though many of the methods previously used have now been superseded, it may be interesting to review some of them. It has already been stated that we have been dissatisfied with angle traction wires. In an endeavour to obtain more rigid control, we first applied a U-shaped loop of flattened German silver to the angle by means of two wires; one limb of the loop was therefore rigidly attached to the bone, while the other, emerging through the skin, pointed forward. This was attached by a sliding tube to a rod somewhat like a Kingsley bar from the mandibular cap splint. The method was reasonably satisfactory except for the length of rod involved. Later, therefore, we carried the bar through the soft tissues of the cheek directly from the splint to the angle. This meant that we were dependent upon the use of a malleable bar for accurate repositioning, and though on the model this is easy to manipulate, in practice it is prone to be inaccurate.

MAXILLARY APPLICATIONS

A simple type of fixation, as illustrated in fig. 5, is frequently used. It may, however, be found that one side of the maxilla is raised too high in relation to the other. Fig. 4 illustrates a method of exerting downward pressure by means of a tube threaded over a cheek wire. The left side is spring loaded to raise it. In this particular instance, retroposition of the maxilla as a whole was corrected by traction with a 4 lb. weight over the foot of the bed. Naturally, such extensive procedures are necessary only when the initial treatment has been inadequate. In this case the maxillary fracture had been ignored for three and a half months and the models show an open and an oblique bite.

A modification of the rigid bar has been introduced by Squadron Leader MacGregor (fig. 6). This gives threaded screw control in all planes. The extremely heavy pressures necessary to replace an old fracture may not be tolerated by this appliance, though the difficulty could be overcome by adding cheek wires to obtain lift at the point of maximum resistance, i.e. in the pterygoid region. For recent fractures it gives a precision of control which is unique.

None of these methods is new in principle, though some of the modifications are relatively recent. They have been brought forward only to point out that combinations of the various standard appliances will cover most eventualities.

Pins

There is, however, one principle which has not previously been applied to the mandible. This is the crossed pin method of external fixation. In previous publications it has been pointed out that this principle does not supersede any of the accepted and well-tried methods. It is, however, most applicable to that fracture which has hitherto been least easily controllable, namely, the fracture at or near the angle with a short posterior edentulous fragment. The actual method of fixation varies in different Units. One type is illustrated in fig. 7. This dispenses with any type of universal joint, whilst still providing universality of movement. The technique of application is simplified by having an assistant. Primary reduction is effected by him from within the mouth. The surgeon marks out on the skin the position of the lower margin of the mandible and the fracture line; he then inserts a pair of pins into each fragment, crossing them as shown. Care is taken to keep close to the lower margins of the bone to avoid tooth roots and the inferior dental canal, and not to penetrate completely through the bone. He then couples each pair of pins to its plate, and now has control of the bone fragments from outside the mouth. He maintains the reduction whilst his assistant checks the bite, and then tightens the screws controlling the intervening fixation bar. Minor corrections can easily be made without subsequent anæsthesia. Fig. 8 shows the three phases in the treatment of a typical fracture.

The advantages of this method may be summarized as follows:

(*a*) Absolute control and fixation without discomfort.

(*b*) Retention of mobility of the temporo-mandibular joint with the maintenance of function and the relative absence of feeding problems.

(*c*) Complete absence of all intra-oral fixation with consequent cleanliness of the mouth.

In our experience with these pins, we have come across a few difficulties. In one case we were unable to get retention of the pins in the posterior fragment. This was probably due to two factors: the patient was an emaciated elderly man, who had been edentulous for many years, and there was marked atrophy of the bone. The other factor—probably less important—was the leverage exerted by the weight of the appliance. This has since been reduced from approximately 1½ oz. to less than ½ oz.

A second difficulty was experienced in an airman who had suffered from an ununited fracture at the angle for many months. The bone ends were freed and freshened and the pins applied. On the third day he complained of increasing and intractable pain in the region of the fracture. No obvious cause could be found. The X-ray appearances did not suggest that the pins in the posterior fragment were near the inferior dental canal. It was thought, however, this must be the case, and that either œdema or a small hæmorrhage was exerting pressure on the inferior dental nerve. The posterior pins were therefore removed, and reinserted nearer to the posterior margin of the ascending ramus with immediate relief. The appliance was subsequently left in position for three and a half weeks without discomfort.

A third difficulty was encountered, though this was when we were endeavouring to assess the potentialities of the method. There was a bilateral fracture at the angle with gross downward displacement of the central fragment. We inserted three sets of pins, one in each fragment. This meant that the weight of the horizontal ramus, together with the stresses of the infra-mandibular muscles and the tongue, were being borne by the torsional resistance of the pins in the posterior fragments. Naturally enough, we did not obtain absolute control, and it was necessary to provide anterior splint support in addition. Thereafter the fractures were treated separately by the same method, with a good result.

So much for difficulties. Other questions arise. Can the method be applied in the presence of infection in the fracture line? We have used it on at least six such occasions with good results, and we have also used it to bridge compound soft tissue injury, without any disturbance. Is the method painful? Does it leave appreciable scars? To these the answer is no. We feel, therefore, that here we have an additional appliance which offers an excellent chance of success in those fractures which have previously been least satisfactory. Pins can be applied either alone or in combination with other methods. Fig. 9 shows pins in position in the posterior fragment; this patient had lost considerable bone in the region of the angle of the mandible following upon an infected compound comminuted fracture due to a bomb injury. Flexion of the short posterior fragment was so marked that function of the temporo-mandibular joint was seriously reduced. This is well shown in the photographs of the patient in fig. 5. The posterior fragment was mobilized and held in position by distraction via a rod to a Gunning splint wired on to the mandible. At first the mandible was fixed to a plaster cap by a central bar; this was later removed and the mandible and its graft allowed to move as one piece. I can think of no other method which would give such efficient control, and it will be noticed that this again is an example of the frequency with which more than one basic method is employed on the same patient.

In giving this brief résumé of various combinations of new and old methods, I have drawn freely upon cases treated by other members of the Unit. To my dental colleagues, Mr. Dudley Buxton, Mr. B. W. Fickling and Squadron Leader A. B. MacGregor, R.A.F.V.R., and to my surgical associate, Mr. Barron, I would like to express my sincere thanks, not only for their courtesy in allowing me to quote their cases, but also for their part in the discussion and planning which has gone towards the obtaining of good results in difficult cases.

Section of Epidemiology and State Medicine

President—E. H. R. Harries, M.D.

[*January* 23, 1942]

Man-Power—Medical Aspects in a World Army To-day

[*Abridged*]

By Colonel D. Gordon Cheyne, O.B.E., M.C., M.D., D.P.H., D.T.M.&H., late R.A.M.C.

In considering the subject of man-power to-day we must reflect on the social conditions in this country during the past twenty-five years, the period towards the end of the Great War and immediately following. The post-war conditions of unemployment, poor housing and limited recreational facilities affected the youth of the country both physically and mentally.

To improve the men physically and alter the outlook of the population as a whole—to make them war-minded instead of pacifist—a tremendous drive was necessary. Amenities in barracks were much improved; in addition to good food and accommodation, mental relaxation was supplied by the provision of lectures, recreations, reading and concerts. The physical standard of recruits was carefully considered and disabilities were more closely assessed so that the flat-footed man did not find himself drafted to an infantry regiment or the skilled draughtsman to a Pioneer Corps.

Shortage of recruits always has had its effects on physical standards. Height and weight may be lowered and more men below recruiting standards are then accepted as special enlistments approved by hygiene officers. So short were we of recruits in 1938 that battalions at home were only at half-strength. The situation was so critical that we were forced to lower our standards. We dispensed with dental standards and provided dentures, we lowered the visual standards for motor transport and Line of Communication Units and took men whose natural vision was insufficient but who could be brought up to standard by glasses which we provided. We accepted men with severe foot defects and employed them in the mechanized M.T. and L. of C. Units.

We took undeveloped and undernourished recruits and sent them to special physical development centres where 80% of them were brought up to recruiting standard. In fact recruiting was the most important part of the work of the hygiene officers in areas. As a result these officers adopted a standard of their own. They knew the common disabilities of that section of the population and assessed their importance in relation to military service in each individual—whether in spite of his disability a man would stand up to military service anywhere in the world, or whether such service might aggravate it. The result of all this was that though the Army ready to take the field was small it had been carefully selected and contained few misfits.

With the coming of war recruiting was entirely taken over by the civil authorities. There were errors of course, due probably in some cases to a lack of proper assessment of the importance of a disability and also to the desire to admit only the cream of the population. Alas, there is not and never was enough cream to go round. When it was decided to categorize the whole Army this lack of appreciation of the importance of disabilities again became evident, and young and inexperienced medical officers were getting busy again actively to dissipate the Army.

The influence of the C.O. is naturally very great and an enthusiastic C.O. anxious for the very best material often finds or tries to explore the medical route for the discharge of what to him are undesirables. This brings me to the matter of selection of material—a subject which assumed an importance much greater than ever after Dunkirk. We were thrown almost entirely on our own resources so that practically all labour for our industrial concerns—notably munitions, agriculture, &c.—had to be found within these islands, while, at the same time, an army had to be raised for civil defence, including fire services—conditions which had never before existed on a similar scale. The standards in the Army inevitably suffered and while certain of its sections had to have first-class material, such as R.A.C. and R.A., material of lower category, mental and physical, had to be absorbed into other Corps. It has been and is very difficult to make C.O.s appreciate this. Naturally everybody wants the best. Remember too that the

call-up age for the Army is from 19 to 45. The R.A.F. takes boys of 17½. This service is much more popular than the Army so we lose the best of the youngsters.

It is more difficult to assess mental than physical ability and the psychologists must try to estimate what a man will be like in three or four months' time. Dull and backward men are undoubtedly a problem, but the rejections are greatly reduced in number of late owing largely to a better understanding on the part of psychiatrists of how such men can be utilized in the Army. The great majority are transferred to Pioneer Units and do well.

Specialists in all branches of medicine and surgery should know something of the duties and work of the soldier otherwise they cannot advise properly upon disabilities *vis-à-vis* such duties. It is interesting to note that in the German Army the psychologists live in much closer contact with the fighting troops, so that they are better able to assess a soldier's mental outlook in that particular arm of the service. Also in Germany each man has a dossier which gives his whole life-history (including medical) from birth; this is of great value to the psychiatrist in summing up the recruit's character and health.

Some years ago I was instructed to observe the effects of prolonged tank life upon physical efficiency. The object of training is to produce physical and mental fitness so that work is carried out at the most economical cost and with a reduction in the time "lag". This is the time between the reception of an order or a stimulus and the correct reaction thereto. The scope of training is not wide even in the R.A.C. and the movements and co-ordination required are not very complicated. A situation is presented which has to be appreciated and then the execution of the appropriate action has to follow. Speed is the all-important factor and training ensures this. I was told then that if officers, trained N.C.O.s, and men, all of whom had completed their training, were pitted against each other in snap-shooting the N.C.O.s would win. If this was so, it excludes education as a dominant factor—education, as we normally accept the term—and puts training first in importance. The best that we can say is that our various tests are an aid in assessing the "trainability" of the men. There are two factors which govern selection of men: (*a*) The increase in mechanized technical units requiring a higher standard of intelligence, and (*b*) Speed of training—two months instead of six. There is no time to train the slow and backward.

When the recruit is accepted for the Army his accommodation is good—not up to peace-time standards, but the reduction in floor space from 60 to 45 sq. ft. per man and in cubic from 600 to about 400 has had no appreciable adverse effects. In the defended localities in this country—coast defence, gun positions, A.A. sites and the like—it has not always been possible to obtain these standards, but on the whole we can view the accommodation of troops with equanimity. Even tentage in winter, provided double tents are issued with linings where possible, impervious floors, fireplaces and plenty of blankets, is much less spartan than it sounds, and the men's health in such tentage in my own experience in the first winter of the war was markedly better than that of men in adjacent barracks. In the Army we endeavour always to ensure separation of heads, and double bunking of barracks has been of great value. I am unable to give many figures of sickness but in my Command the total admissions to military hospitals for tonsillitis, bronchitis, pneumonia, and influenza in the first six months of 1941 amounted only to about 8 per 1,000 of the population. This figure excludes epidemic catarrh which in the mild form experienced was treated at reception stations.

Feeding of the Army continues satisfactorily with the advice of nutritional experts. Deficiency diseases are practically non-existent in the Army in any part of the world and the issue of vitamin preparations has been made only in very few instances. Recently tests to ascertain the degree of vitamin C saturation in groups of soldiers living under various conditions have been satisfactory. Improvements in feeding and messing have resulted from the appointment of catering advisers and the establishment of an Army Catering Corps, but it is constantly stressed that the Medical Officer should be the scientific adviser in his own unit. Schools of cookery are established and the students include Commanding Officers who not only prepare food but have to eat it. These schools are concerned with cookery all over the world from Salisbury Plain to the Desert and a lecture on the scientific aspect of messing and feeding by a hygiene specialist is included in each course. Special compact rations for special purposes where lightness and high nutritive value are of supreme importance have also been evolved.

An important part of the organization is the exclusion from kitchen staff of carriers of diseases, notably dysentery and the enteric group, and the strictest precautions are being taken with prisoners of war who may come to this country similarly to exclude intestinal carriers and other disease carriers. This should constitute an effective barrier against infection of the civil population. I may say the incidence of dysentery and enteric fever has been exceptionally low even during periods when there was a considerable incidence amongst the civil population. Inoculation remains a sheet anchor in the Army.

The training of the soldier is supervised by medical officers whose duty it is to impress upon Commanding and Training Officers the necessity of setting a pace for the average and not the super-enthusiast, of watching for signs of breakdown, and of attention to weights, avoiding strain and overloading the man on marching. I consider that the old standard of being able to march 20 to 25 miles in full kit day after day for a week must go, good as the standard was, but on many occasions the soldier will still be called upon to march to a destination and fight. The medical aspect of correct loading of the soldier, carriage of equipment as well as weight and distribution on the man, are constantly being watched and the importance to hygiene of new equipment as well as new developments in military tactics is ever in the minds of the various departments concerned.

I consider every medical officer should have a spell of regimental duty before going on to a hygiene appointment, for the application of hygiene knowledge differs immensely in civil and military practice. Every Field Hygiene Section mobilized on a divisional basis now runs a school which is an Army School of Hygiene in miniature. Instruction is given by the O.C. and his N.C.O.s; many of the latter are ex-civil sanitary inspectors. These schools are attended by the sanitary and water duty men of units. Special courses are held for medical and other officers and lately we have included A.T.S. officers and auxiliaries, and they are essentially intended for Field Service. We are also teaching elementary tropical sanitation, and lectures are given at other schools of instruction and O.C.T. Units, in the hope that if we can instruct these officers as early as possible greater benefits may result.

Propaganda films on such subjects as water purification, malaria prevention and the fly, louse, &c., have been prepared in addition to the issue of certain Army propaganda posters.

Certain organizations have been built up to restore to the Army man-power which has been temporarily lost to it, such as Convalescent Depots, Medical Examination Centres, and Physical Development Centres. Red Cross Convalescent Hospitals, though not under Army administration should be included. I would like to pay a tribute to the Emergency Medical Service. I look on hospitals as a most important element in the conservation of man-power, for on the skill of the staff depends the man's rapid return to duty and his saving to the Army. Our relations with the regional authorities of the Ministry of Health, including Medical Officers of Health are close and cordial and we owe them much.

The Red Cross Convalescent Hospitals receive our patients and perform the first part of their rehabilitation. From there or directly from a hospital, civil or military, all patients—with a few exceptions—proceed to a military depot where they are trained by stages to return to full duty with their units. The staff includes P.T. experts, masseurs, &c., and the command specialist in physical medicine, as well as the consultants in this branch, watch over the whole of the activities. The training programme is carefully graduated and work of first-rate importance is achieved.

The Medical Examination Centre is a new feature and it is as yet too early to assess its value. It is intended that men who are considered unfit for any form of military service, either while in their units or after being in hospital, should be sent there for medical boarding. The hospital cases are men fit to walk, able to look after themselves, and on ordinary diet. The real hope is that careful examination and medical boarding by experts may result in a saving of personnel by placing them in suitable jobs in the Army. As regards such men in units, careful boarding by the Civil Panel should exclude them to a large extent at the outset, and discharges from the Service should be rare. Expert knowledge of their possible utilization in the Army in some capacity is essential on the part of the examining board. The bed situation in hospitals is also helped by such a centre. It has been separated from Convalescent Depots, as it seemed undesirable to introduce an element where discharge from the Army was dominant into a unit where the desire for fitness to carry on should be the all-important outlook.

The Physical Development Centre is a revival of the centres which existed at Canterbury and Scarborough before the war, and which were so conspicuously successful. They received the "underweights" from depressed areas and men with various defects, mainly foot disabilities, spinal defects and other minor curable afflictions. Similar work is being done at this new centre with considerable success, especially in the case of undernourished and underdeveloped individuals. Flat-feet cases are responding to treatment. Much of the success of the centre must depend on the selection of the material sent to it—70% of the cases have their category raised. The ideal of course, is some centre where all the intakes would come and where they would be examined, questioned, analysed, scrutinized, categorized, and where every man would be put into that particular niche which fitted him. This is perhaps Utopian, but even with the present system, a man should ultimately find that niche and stay there, provided always, C.O.s would realize that the stream of man-power is not a mighty torrent and that the quality is intimately bound up with the many calls upon the man-power of the country.

The response to inoculation against typhoid, and paratyphoid A and B, in this country is satisfactory, and its value is proved. The same may be said of vaccination against smallpox, but here we have the complicating factor of large numbers of the entrants unprotected by previous vaccination in infancy, or at any other time. Their reactions are in many cases severe, with consequent interruption in training. Here again the response is good, and this is of great importance considering the fields of action in which the Army may find itself. When troops go to yellow fever countries, they have the advantage of protection given in this country against the disease. Special malaria units have gone to the East. Special arrangements for disinfestation will accompany units where there is a risk of typhus. Protection against tetanus is now a routine measure, and cholera inoculations are available whenever specially called for. We are carefully watching typhus inoculation experiments. Every factor for the spread of the commoner zymotic diseases was present in the first year of the war, and if we except German measles we have had practically nothing in spite of all forebodings. Our cerebrospinal fever figures compared favourably with civilian figures, and we have never had anything more than sporadic and widely separated cases. Now we have a good organization for the treatment of major infectious diseases, and should it be necessary we are prepared to convert some of the smaller hospitals for use as infectious hospitals. Every Station has a plan for dealing with outbreaks of the milder infections.

We have established centres for treatment of scabies all over the Command, and these are supervised by our skin specialists. A large number of beds are continually occupied on this account. The recent work of Kenneth Mellanby is most interesting and bears out the Army view that scabies is a disease of very close contact. We are convinced that our men and women are acquiring the infection while on leave. I can sense my civilian confrères' eagerness to tell me that the reverse is the case, but here my American colleagues of the Harvard Red Cross Hospital Unit tell me they have been following up cases in their homes and have found entire families affected.

This subject of contact between the civil and military assumes supreme importance when the question of louse-borne diseases is discussed. We should conduct a most strenuous campaign in all classes of the population on the danger of lice infestation. There seems to be an appalling ignorance of this; and the incidence of head infestation by lice, and nits, amongst our Service intake, i.e. recruits, has been, at times, alarmingly high. If the cause of this, as it well may be, is partly the fact that the modern method of women's hairdressing prohibits the washing of the sides and back of the head, because of the danger of spoiling a coiffure, then surely it is time that this style was laughed out of existence. I feel that we are losing a first-class method of propaganda.

We cannot disregard the head louse as a possible transmitter of typhus. At present we are trying to make a census of cases of pediculosis amongst troops. It is quite obvious that the louse, if not destroyed, can become a much greater dictator than any human we have yet known, and can take a much greater part in altering the destinies of nations than any conference of humans. Every Army M.O. should read Zinsser's book (1935, "Rats, Lice and History", London). Plans must be ready, civil and military authorities must act in the closest co-operation. In the Army, in this country, control should be easy, if conditions remain substantially as at present, but abroad the problem may be vastly different, if populations have—as they well may—to adapt themselves to an entirely different method of life, with all the standards now normally accepted drastically altered. It is only by education of *all ranks* that this can be assured.

The importance of the A.T.S. organization becomes greater daily. The special problems of enlisting bigger numbers of women have been largely overcome, and barracks, camps and reception stations have been adapted for their use. Difficulties arise with the small parties who are attached to units, but the larger depots are easily arranged. Conditions as regards mixed batteries in Southern Command are satisfactory, and the health of the auxiliaries has been good. They are being carefully watched in order to see what, if any, deleterious results accrue from their special duties. It is gratifying to note that the incidence of venereal disease has been negligible in this Command. In these mixed batteries I saw no signs of any deleterious effect on their health, physical or mental, and—perhaps this is a secret—Commanding Officers of the old school, who viewed such innovations with horror, are being completely won over and appreciate the quickness and general suitability of women for this work. Recent intakes of A.T.S. in my Command are working very satisfactorily and smoothly. The services of women medical advisers at Command Headquarters are much appreciated.

The British Army of to-day can only be of a certain size, because of the demands of industry and agriculture, and because of the limitation of the quantity of armaments which can be produced. We have not been faced with a similar problem for nearly two centuries.

Section of Urology

President—G. E. Neligan, M.C., F.R.C.S.

[*February* 26, 1942]

Experiences with Phenothiazine as a Urinary Antiseptic

By William H. Graham, F.R.C.S.

(*In absentia* read by T. J. Millin, F.R.C.S.)

Introduction

Phenothiazine is the parent substance of the thiazine dyes, and has a chemical formula closely related to methylene blue. Oral administration results in the urinary excretion of phenothiazine and its two oxidation products, thionol and leucothionol, part of the leucothionol being in some loose chemical combination. Leucothionol is spontaneously oxidized to thionol, which imparts the characteristic red colour to the urine, and gives it its bactericidal properties. Thionol-leucothionol is a reversible oxidation-reduction system similar to methylene blue and its leuco base.

Thomas, DeEds and Eddy, of San Francisco, showed the bactericidal properties of urine containing thionol, and because of the low toxicity after oral administration of phenothiazine, as shown by growth curves and blood picture changes, DeEds, Stockton and Thomas (1939) considered it justifiable to undertake clinical trials with it. They carried out this trial on two groups of patients. The first group of 61 patients was given phenothiazine alone. The second group of 31 patients was given phenothiazine in combination with ammonium chloride. The acid reaction of the urine, especially in the pH range of 4·5—5·5, facilitated the liberation of the leucothionol held in combination, and this oxidized to thionol increased the active bactericidal properties of the urine.

In the first group 33 had chronic urinary tract infection complicated by obstructive lesions. Many had previously received prolonged courses of treatment, both local and general. Sixteen had acute urinary tract infection. The types of bacterial infections were varied, covering *B. coli*, streptococci and staphylococci and the typhoid dysentery group. This could be taken as a good test of the efficacy of phenothiazine as a urinary antiseptic. No patient was considered as cured who had not been observed for a minimum period of four weeks following the cessation of administration of the drug. Others with temporary freedom from symptoms, or apparently cured and observed for less than four weeks were classed as "improved".

10 of the 16 acute infections were cured, 5 of the 35 chronic infections were cured and 20 more improved. Only eight of the 49 patients in this group using phenothiazine alone failed to secure relief from their symptoms. The average daily dose of phenothiazine was 1·33 g. during an average period of 7·4 days. The average total dose was 9·99 g.

In the second group of 31 patients, ammonium chloride was administered with the phenothiazine. A daily dose of 1·9 g. of ammonium chloride was found sufficient to maintain the optimum pH value of the urine, namely between 4·5 and 5·5. The increased thionol content was shown by the intensity of the red colour. 20 of the patients had acute urinary tract infection, a higher percentage than that in the first group. The authors summarized their findings, stating that 25 out of the 31 were symptomatically cured in an average time of three days. The dose of phenothiazine was approximately one-half that used in the first group, who received phenothiazine without ammonium chloride.

During this investigation of 61 patients, no undesirable effects or complications arose which could be attributed to the drug. There were no signs of gastro-intestinal upset nor of renal irritation. The direct Van den Bergh reaction was never elevated, and any rise in the indirect Van den Bergh and icteric index could be attributed to the colour of the dye. Liver function tests showed no change. Blood-counts were done in 19 of the patients. Three patients developed a secondary anæmia after receiving an average total dose of 23·5 g. In one patient this anæmia was marked after nearing 19·9 g. The red

cells had fallen from 4,410,000 to 1,510,000 and the hæmoglobin from 84% to 34% with a white cell increase from 11,250 to 21,650. The authors concluded that anæmia produced by phenothiazine is an exceptional and rare occurrence, but advised that the blood should be examined periodically and any evidence of anæmia should be the signal for stopping medication. After a maximum total dose of 15 g. a rest-period was advised. These findings led to the hope that an alternative to sulphonamide (with its subjective symptoms of nausea and depression) had been found to overcome those chronic infections resistant to the usual line of treatment consisting of increased fluid intake and change in the reaction of the urine, to which many cases of urinary tract infection respond. Accordingly it was decided to repeat this clinical trial with phenothiazine. With the support of the Research Committee of the London County Council, we had at our disposal a large number of suitable cases which could be kept under close observation.

Phenothiazine in tabs. 0·5 g. were given three to four times daily. The urine was maintained at a pH 4·5 to 5·5 by tab. ammonium chloride 0·5 g. q.i.d. before administration of the phenothiazine, and then on alternate days. Bacteriological examinations were made during the course of treatment. Blood-counts were done, and after six days of treatment were repeated unless symptoms indicated an earlier examination. Only 8 cases had been subjected to the trial treatment when the alarming blood pictures and the same small percentage of improved cases showed that continuation was unjustified, and the trial was abandoned.

CASE I.—F. A., female, aged 20 years. Gave a history of dysuria and frequency at intervals for the previous twelve months. Bacteriological examination of the urine and culture showed numerous colonies of paracolon bacilli. Pyelography showed no abnormality. Cystoscopy revealed slight trigonitis. Guinea-pig inoculation for tubercle bacilli was negative. A course of sulphapyridine gave no relief. Phenothiazine was given a trial, 4 tablets being administered daily with ammonium chloride. After seven days' treatment the appearance of the patient suggested an increasing anæmia. Blood examination showed that the red cells had fallen from 5,680,000 to 2,960,000 and the hæmoglobin from 108% to 54%. In all, 16 g. of phenothiazine had been given without improvement in symptoms or in the bacteriological content of the urine. The anæmia responded well to iron medication, the blood-count and hæmoglobin percentage returned to normal within one month. This suggested that the anæmia was of a toxic nature and that the bone-marrow was unaffected.

CASE II.—C. J., male, aged 67 years. Admitted suffering from acute retention of urine due to prostatic enlargement. Catheter drainage was instituted *per urethram*. The urine was heavily infected. Bacteriological examination showed a heavy growth of coliform organisms. Urethritis developed, and as the general condition of the patient necessitated it, suprapubic cystostomy was performed and the vasa deferentia divided.

The wound became infected and suppurating, and a profuse discharge came from the site of division of the vasa. The urethritis persisted. Phenothiazine 0·5 g. was given four times daily along with ammonium chloride. After seventy-two hours there was a definite improvement in the condition. The medication was continued for eighteen days, by which time the suppuration had ceased, the wounds had healed, and the urine was sterile. 36 g. of phenothiazine had been given. The patient looked anæmic, and blood examination showed that the R.B.C. had fallen from 4,350,000 before treatment to 3,070,000, the hæmoglobin from 68% to 54%. The phenothiazine was stopped and iron medication begun. The patient became more anæmic, as was shown by blood examination eight days later when the red cells had fallen to 2,880,000 and the hæmoglobin to 42%. A blood transfusion was given, after which the patient made a rapid recovery. The infection in this case apparently responded to the phenothiazine.

CASE III.—W. O. F., female, aged 23 years. This woman was symptomless, but had a heavy *B. coli* bacilluria persisting after an attack of pyelitis. Pyelography and cystoscopy revealed no abnormality in the urinary tract. A daily total dose of 2 g. of phenothiazine was given with ammonium chloride. Repeated bacteriological examinations showed no change in the growth of *B. coli*. Treatment was continued for thirteen days, 26 g. of phenothiazine having been given. Blood-count examination on the twelfth day of treatment showed a relative lymphocytosis and W.B.C. of 5,600 with polymorphs. 29% and lymphocytes 61·5%. The treatment was discontinued. The *B. coli* infection had not responded to phenothiazine.

CASE IV.—M. N., female, aged 51 years. Complaining of frequency and dysuria. Urine gave a heavy growth of *B. coli*. On cystoscopy there was well-marked trigonitis. Phenothiazine was given, 0·5 g. four times daily, along with ammonium chloride. After three days the symptoms definitely improved, but bacteriological examination showed no difference in the urinary infection. In six days, owing to nausea, sweating and

depression, the drug was discontinued. There was still a heavy growth of *B. coli* in the urine. There were no blood changes. A total of 12 g. of phenothiazine had been given.

CASE V.—R. G., male, aged 3½ years. Admitted with *B. coli* bacilluria. Phenothiazine was given, 0·25 g. q.i.d. In three days the urine was sterile. Blood examination the same day revealed a relative lymphocytosis. The white cell count was 8,600, of which 69·5% were lymphocytes, 28% being polymorphs. In view of this blood-count the drug was discontinued. The child showed no toxic symptoms and was discharged from hospital. Twelve days later he was readmitted. There was an icteric tinge of the conjunctiva and general wasting. The abdomen was distended and tympanitic and the liver was enlarged 1 in. below the subcostal margin. The blood examination was repeated, showing a white count of 5,900, 40% polymorphs. and 54·5% lymphocytes, the lymphocytosis being less marked. The red cells appeared to be unaffected. Glucose was administered, and in seventeen days the condition had completely cleared up, but the relative lymphocytosis remained unchanged. This was considered to be a toxic jaundice and was directly attributed to the phenothiazine medication.

CASE VI.—C. W., male, aged 59 years, suffering from infected bilateral hydronephrosis. Both kidneys were enlarged and tender. The urine was thick with pus and contained a heavy *B. coli* infection. The patient had a persistent hiccough and became very drowsy. Phenothiazine 0·5 g. q.i.d. was given. The blood urea was 201 mg. per 100 ml. Phenothiazine 0·5 g. q.i.d. was given. He showed a steady improvement, the blood urea falling day by day and the urinary infection decreasing. The phenothiazine was continued for seven days, a total dose of 14 g. having been given. Blood-counts showed a fall in red cells to 2,030,000 and a 40% hæmoglobin estimation. The drug was discontinued. Blood transfusion was given and with iron medication the blood picture returned to a satisfactory level. As far as one could judge, the urinary infection responded to phenothiazine, but a marked toxic anæmia followed.

CASE VII.—E. H., female, aged 37 years. A *B. coli* bacilluria complicated this patient's convalescence following subtotal hysterectomy and bilateral salpingo-oophorectomy for bilateral tubo-ovarian abscesses. The routine phenothiazine medication was carried out over eight days. A total dose of 16 g. was given with no effect on the urinary infection, which still showed a heavy growth although the symptoms were alleviated. There were no blood changes in this case.

CASE VIII.—M. H., female, aged 38 years. Repeated attacks of left loin pain associated with frequency and dysuria had given this patient much distress over the past twelve months. Investigations revealed a double ureter and pelvis on the left side, complicated by a *B. coli* infection. Phenothiazine and ammonium chloride were given for seven days without any effect on the urinary infection, as shown by repeated cultures. In all, 14 g. of phenothiazine were given. There were no blood changes of any note.

CONCLUSION

In this small series of 8 cases, only 2 showed improvement in the urinary tract infection. 6 cases sustained a severe degree of R.B.C. destruction. Two cases of relative lymphocytosis with a low polymorphonuclear cell-count suggested that the bone-marrow had not escaped damage. Toxic hepatitis followed in 1 of these 2 cases. The conclusion was reached that phenothiazine has no place in the treatment of urinary tract infection.

[I should like to express my thanks to Messrs. Burroughs Wellcome, who supplied the drug, and to Dr. Prescott, of the Wellcome Research Laboratory, for his support in initiating the trial. My thanks are also due to the Medical Superintendents of St. Mary Abbots and Fulham Hospitals, and the staff of the Group Laboratory, for their kind co-operation.]

REFERENCE

DEEDS, FLOYD, STOCKTON, A. B., and THOMAS, J. O. (1939), *J. Pharmacol. & Exper. Therap.*, **65**, 353.

In the subsequent discussion it was agreed that many advertised urinary antiseptics were spurious. The only effect they had was to show some colour in the urine and as antiseptics they were useless.

The speakers were: The PRESIDENT, Mr. A. CLIFFORD MORSON, Mr. E. W. RICHES, Mr. J. T. CHESTERMAN.

Refractory Ulcerative Cystitis

By A. Wilfrid Adams, M.S.

Terminology.—The condition of refractory ulcerative cystitis has been called after names of surgeons and by somewhat poetic titles. It would be advantageous for the sake of popularizing the diagnosis in the medical mind to group together under one clinical title—such as heads these remarks—the lesions known as Fenwick's solitary ulcer, Hunner's elusive ulcer, pan-mural, interstitial cystitis, &c. The disease may be uncommon but early recognition is important, if we are to save its victims from a pernicious scourge. It is well to remember that the rarity may be more apparent than real. If the possibility of the disease is not in his mind the doctor will not, in milder cases, feel moved to send the patient for the revealing cystoscopy. A suitable title will help the doctor to recall that there is an organic cause of refractory cystitis which is liable to rank as trivial or functional disease because the customary changes in the urine are wanting and, instead of physical deterioration, there is often increase in weight. The simple truth is at present so obscured by a multiplicity of names that we can scarcely blame the practitioner for the protracted histories of suffering which the patients usually tell us.

Symptoms.—The multiple type of ulcer (Hunner [1]) occurred in five of the present seven cases reported, all women, ages 36, 21, 68, 58, 44 years. The solitary ulcers (Fenwick [2]) were in men, ages 62 and 66 years.

The complaints start rather abruptly with frequency and, usually, pain at the end of micturition. Hæmaturia, which may be heavy, occurs at times in about half the cases. The dysuria is apt so to increase that the patient is tied to the house. In addition, spontaneous stabbing pains may be felt through the pubic and rectal regions and be aggravated by mechanical causes, e.g. movements or by lateral recumbency. The patient may sense the exact locality of a sore or sores in the bladder itself. One, F. W., calls such "ulcers", as the pain derived reminds her of the sore ulceration in the mouth to which she is also prone. In the sixth year of her illness the pain extends as an ache through both legs to the great toes, especially the left.

All the patients were of average physique and a psychopathic taint only manifested in one (D. M. A.).

The urine looks inoffensive and the pathologist merely reports pus and red blood cells. Later, when necrotic changes are going on, *B. coli* and streptococci appear. Guinea-pigs were inoculated in four cases with negative results.

Urography.—In six out of seven patients pyelography was used. The two cases of solitary ulcer showed right hydronephrosis, slight in W. B. (pelvis × 2), and in the man R. P., it was definite (pelvis × 4). In none did it suggest a causal relationship, and is discussed later.

(a) the multiple type of ulcer

Cystoscopy is facilitated in these irritable bladders by low spinal anæsthesia.

Stretching the ulcers is wont to provoke bleeding and, therefore, calls for cautious filling of the bladder.

The posterior hemisphere well above the trigone is the site of the lesions. In one case (D. G.) there was an appearance akin, but not due to, Koch's infection at the left ureteric orifice. This was swollen and appeared fissured, whilst round it the mucosa was studded with little tubercles. In moderate cases two or three little irregular patches of slightly raised hyperæmic mucosa are visible on a background of ordinary straw colour. They may amount to little more than trivial marks resembling spider nævi, even in cases with long histories. With time or subsequent to diathermy the inflammation tends to develop into ridges on which ragged linear ulceration develops. Attached to the ulcers fibrinous strands are often seen, looking like cobwebs. Issuing blood may appear in the form of waving streamers and in one instance on pressure with an electrode, creamy pus was seen. In advanced cases the areas are broad with shallow ulcerative erosions, as if a mouse had nibbled the bladder wall. Phosphatic incrustation may be seen.

Case Reports : I.—D. M. A., 36 years, spinster, gave a history of acid water for two years and marked frequency, day and night. There was an interval of six months' return to normal between the onset and the subsequent symptoms. She felt " acid run round the bladder after meals ". Bladder washes greatly aggravated the symptoms. The urine was faintly red, although the patient had not observed any abnormality. When, in November 1940, diathermy was started, two ragged granulating ulcers were present ¾ in. in diameter, on the posterior wall. The dysuria abated to negligible proportions but there was recrudescence, which tonsillectomy in the spring of 1941 did not benefit. By 23.7.41, three ulcers were seen and more radical measures were likely to be necessary. She developed mild delusions for a time, but on 23.2.42, the doctor reports " much improved and happily teaching ".

Conclusion.—One is left with the impression that the condition is barely controllable by diathermy, although the last application has effected notable improvement.

II.—The woman D. G., 21 years, came to me first on 31.3.37. Like the preceding case, she was single and well nourished. There was slight suprapubic tenderness. Frequency had developed during the previous four years and there had been hæmaturia. A course of salvarsan gave no persistent benefit, so, to a large red jelly-like patch on the dome of the bladder, diathermy was applied. Hers was the ureteric orifice which, at the next cystoscopy, somewhat resembled tuberculous infection, but investigation refuted the idea. By 28.1.38, operation and excision of the affected area in the dome of the bladder became necessary. It was an elevated thickening of the submucosa, like a button about ¾ in. in diameter but not ulcerated. The histology conformed with that of Hunner's ulcer. She appeared cured and looked radiantly well on 30.5.38, but two days after marrying (against my advice) in October 1939, she developed a frequency which has confined her to the house ever since. The last cystoscopy was in 1940 when a large part of the posterior bladder wall showed ragged ulceration surrounded by a raised, rolled edge. She still (9.2.42) rejects proffered transplantation of the ureters.

Conclusion.—Her story includes a disappointing relapse and demonstrates the pernicious nature of the lesion, the patient's imprisonment by it and the only likely cure to lie in the transfer of the bladder function to the bowel.

III.—In the case of L. H., 68 years, a widow who came on 8.3.40, pain and frequency had troubled her for four years. Occasional stabbing pains into the rectum also occurred. The bladder showed areas of condensed vascularity with tiny petechial blobs on the capillaries, like terminal buds on twigs, as well as woolly patches of mucosa with central ragged ulcers and tags of granulation tissue. Neither diathermy nor a course of salvarsan prevented the lesion extending round the back of the bladder in the characteristic irregular crescent from about 1 in. above the right to a similar level above the left ureter. The frequency is aggravated by jolting in buses or by agitation. She was still able to get out of doors a little, till a month ago.

Here again, ureteric transplantation seems preferable to leaving the patient in her miserable state.

[POSTSCRIPT (15.4.42).—Since writing the above bladder lavage with silver nitrate has been followed by marked relief.]

IV.—Mrs. M. C. S., 58 years, similarly for four years suffered from dysuria before reaching me. Hæmaturia had developed and she passed bits of flesh in the water which had a heavy *B. coli* infection. Cystoscopy showed multiple shallow erosions and an appearance simulating cancer. Suprapubic cystostomy was performed for biopsy and with a view to possible ureteric transplantation. Shallow ragged ulcers without any induration or thickening were found. Dr. A. D. Fraser reported on the excised portion : " non-malignant ulceration conforming with Hunner's type." She refused further treatment and I am unable to obtain subsequent reports of her condition.

V.—Miss F. W., 44 years, gave in February 1939 a history of three years' chronic cystitis and recent inability to lie on the left side. At cystoscopy the patches of cystitis bled and prevented ureteric catheterization but this was achieved subsequently with negative findings. A course of salvarsan was given without benefit. A year later two small hæmorrhagic areas only were seen near the dome of the bladder posteriorly, with a tendency to polyposis but no visible ulcer. On 4.2.42 never having had operative treatment by the cystoscope or otherwise, she said the pain and frequency were getting worse and she had not left the house for about a year. In addition to the dysuria, aching in the bladder spreads down her legs, especially the left one, to the great toes. Her weight has increased despite the suffering.

At cystoscopy, 18.2.42, about 6 oz. of clear urine ran out and the ureteric orifices were normal. An irregular arch of chronic ulceration extended round the posterior wall of the bladder in the usual site. On the right the surface looked greyish-white and irre-

gularly eroded, as if nibbled by a mouse. The margin was deep red in places. The central region more resembled icing sugar, while to the left was a white area decorated by bare interlacing bars of muscle, denuded as by exfoliative cystitis and neatly bounded by an even, rather geometrical margin. This part simulated an abiotrophic lesion rather than an advancing infective or malignant ulcer. Inspection was partly hampered by instrumental defect and, at the close, streamers of blood suddenly appeared from the white ulceration. The patient complained of pain and shortly after vomited. As this was happening a rent became visible through which the shreddy margins tended to be carried into the dark space beyond the bladder. Evidently erosion had thinned the viscus which could not withstand continued distension. Prompt laparotomy revealed the entry of lotion into the abdomen but no tear was visible in the peritoneum over the bladder. The latter was opened, the ulcerations were probed and a hole found on the left side, but how it communicated with the peritoneum was obscure. The perforated area of the bladder was excised and a suprapubic drain installed. Dr. Fraser reports the presence of pyuria obviously originating in some other process than the mild infection with *B. coli* and streptococci would explain. Histology showed no evidence of neoplasm and no organisms could be demonstrated.

Here is another instance of the protracted nature of this disease, which has culminated in pathological rupture of the bladder and provides a warning of the risk of this very rare complication of cystoscopy. It further emphasizes a pathological feature notable in two other of these bladders exposed at operation, viz., the absence of any protective thickening of the bladder wall or peritoneum in advance of the ulcerative process.

[POSTSCRIPT (9.4.42).—This patient's wound is healed. Micturition is painless and occurs only eight times in 24 hours. She has acquired a vigorous, healthy, happy appearance and walks well, which is a remarkable sequel to years of invalidism culminating in a grave calamity.]

Review of Five Cases of Multiple Type of Refractory Ulcerative Cystitis

(1) All are women, three being single.

(2) Ulceration tends to develop an irregular crescentic distribution across the upper zone of the posterior bladder wall. What bearing has this on ætiology? Is it a local peculiarity of vesical blood supply that renders this part prone? The contiguity of the uterus is conceivably influential but no gynæcological disorders were noted.

(3) The usual absence of thickening in advance of the ulcers received poignant proof by pathological rupture during one cystoscopy.

(4) Salvarsan has not helped. Cystoscopic diathermy relieves but relapse is common. This may also occur many months after an apparently successful excision.

(5) In consideration for the patient's feelings and lest her healing powers become exhausted, there should be timely resort to ureteric transplantation.

(6) Though uncommon, the disease demands earnest attention, for it is apt to impose a sentence of most painful penal servitude on its victims.

(B) SOLITARY ULCER

For clinical purposes, and since neither the multiple nor solitary type is common, this variety is well included under the generic clinical title of " refractory ulcerative cystitis ".

Two examples are reported—men in the sixties. They complain to the doctor of the same protracted symptoms as the women, viz. relentless frequency at the onset and, later, scalding micturition. There was intermittent hæmaturia in one (W. B.).

At cystoscopy the pathological distinction from the multiple type becomes apparent. As the appearances of the lesions were not uniform it seems better to describe them with the individual case reports.

Mr. W. B., 66 years, came in September 1940 with a history of half-hourly frequency and hæmaturia on four occasions. Pain had only supervened since instrumentation at another hospital a month before, up to which time he was working. There was nothing in the family history bearing on the illness. Physique was fair for his age. The urine was that of acute cystitis with an infection of *B. coli* and streptococci. Urography showed competent kidneys but there was a slight suggestion of stasis and kinking in the right ureter which may have a bearing on later complications.

At cystoscopy the bladder capacity was about 6 oz. A sessile plaque of growth, rounded and about 1½ in. broad, with surface half clouded by fluffy material, was seen rising from about the middle of the posterior wall, an inch from the right ureter. The catheter passed readily through the right ureter, the wide mouth of which appeared retracted under an anterior ledge. The prostate was somewhat conical. On 6.6.41 partial cystectomy and vasotomy under spinal anæsthesia were undertaken. The lesion appeared as a slight thickening, notably rough compared to the normal mucosa around. It was removed with a ½ in. belt of healthy tissue and naked-eye section showed the submucosa $\frac{1}{12}$ in. thick in contrast to the normal $\frac{1}{32}$ in. My cystoscopic diagnosis of carcinoma was invalidated. Fashioning a bladder out of the small remains of the organ was an exacting task. Dr. Fraser reports: "This is a large ulcer with a base formed of exuberant subacute granulation tissue. No organisms can be seen and there is no evidence of carcinoma. At one point there is a suggestion of tuberculous infection but on the whole the appearances are those of a simple ulcer of the bladder and would agree with Hunner's ulcer."

Suprapubic leakage continued and I blamed the prostate. This was treated by resectoscopy in September 1941 and only recently has a suprapubic sinus become dry. Sepsis is present now (15.4.42) in his right urinary tract to whose slight structural imperfections allusion was made above. Right nephrectomy is needed because although his temperature and pulse remain normal between them, he has recurrent rigors and vomiting with some tenderness in the right loin every few weeks. The urine shows a little pus, there is hourly frequency but otherwise he is doing well. Another surgeon who cystoscoped him in November 1941 saw satisfactory healing within the bladder.

The second case of solitary ulcer occurred in Mr. R. P., aged 62, a fitter in aero works, who came in September 1940 with a history of frequency $\frac{D\ 20}{N\ 10}$ for ten years. There was no remission of symptoms, yet he persevered at work. The trouble started a few months after a sudden retention had required relief by catheter. The urine was always clear and micturition painless until about two months before admission. Since then, so acute was the dysuria that his mates had thrice found him faint on the floor of the water closet and thick white jelly appeared in the urine.

He was a spare active man, very tender over the right kidney and slightly so over the bladder. Urography showed right hydronephrosis (pelvis × 4) and a systolic bladder. *B. coli* and streptococci were present in the urine.

At cystoscopy, the small hyperæmic bladder showed a deep ovoid ulcer about the site of the right ureter and measuring ½ in. in its long (vertical) axis. It had a grey necrotic base with an edge raised and, at the lower end, resembling epithelioma. Indigo-carmine was injected but no efflux seen from either ureter fifteen minutes later and the latter defied detection.

16.9.40: Exploration of exterior of bladder and right ureterostomy. The bladder was first completely divested of its peritoneum. It was thickened uniformly but supple. The region of the ulcer did not feel like neoplasm. Right ureterostomy appeared essential and allowed catheterization. At the same time a portion was removed for biopsy. Both a guinea-pig test and histology excluded tubercle, and time carcinoma, for he soon became very well. Two months later the pelvis of the right kidney was normal on pyelography. Ten months later he felt perfectly well, the bladder held ¾ pt., and was normal on cystoscopy.

On 16.7.41 uretero-colostomy replaced his external fistula. After a somewhat stormy time he healed and has been working. On cystoscopy, 11.2.42, the right ureteric orifice was both visible and normal. 1 in. above it is a triangular recessed area which is white and smooth and the only vestige of the menacing ulcer which tyrannized over him for ten years. His motion, somewhat soft, does not come away too frequently. Residual urine is clear and less than 1 oz. Micturition is normal but *B. coli* infection persists. He seems perfectly well clinically.

Review of Two Cases of Solitary Ulcer

(1) Presumably the two cases represent the early proliferative and the late non-specific ulcerated stage of interstitial cystitis—in Fenwick's view somewhat analogous with peptic ulcer.

(2) In contrast with the multiple ulcers in women this lesion is solitary, more basal and there is marked proliferation in advance of the ulceration. The different sexual anatomy possibly accounts for this variation in men and women.

(3) It appears to be more amenable to ordinary surgical treatment than is the type with multiple ulcer.

(4) The efficacy finally of resorting to diversion of the urine; even when this was done unilaterally it proved curative in one case.

(5) In other respects the conclusions on the multiple cases apply.

ABSTRACT

(1) Refractory Ulcerative Cystitis is proposed as a title for covering this group of rare but kindred ills obscured at present by a medley of names and apt to be neglected.

(2) From this revised nomenclature that clinical clarity may result which is needed to keep the disease more in the doctor's mind and so shorten the long history of misery these victims usually suffer and which amounts to little less than most painful penal servitude.

(3) Seven cases are reported. Five of multiple variety in women and two solitary in men. Symptoms, pathology and treatment are reviewed.

(4) Outstanding frequency and pain sharply contrast with slight pyuria in refractory ulcerative cystitis.

(5) While it was distended during cystoscopy, pathological rupture occurred in one bladder with advanced multiple ulceration.

(6) A plea is made for research into the ulterior cause of this primary inflammatory infiltration of the bladder wall. Noteworthy are some points of resemblance to peptic and colitic ulceration.

REFERENCES

1 HUNNER, GUY L. (1918), *J. A. M. A.*, **70**, 203.
2 FENWICK, E. HURRY (1900), " Ulceration of the Bladder ". London.

DISCUSSION.—Mr. A. CLIFFORD MORSON made a point of the ambiguity of the cystoscopic appearance, the disease simulating malignant ulcer of the bladder. He emphasized the need for research on the pathological side.

Mr. E. W. RICHES mentioned the method of treatment in elderly women beyond the age suitable for operation of repeated cautious distention of the bladder.

Mr. T. J. MILLIN supported this, saying that in his experience he had found it of good effect.

The meeting agreed that ureteric transplantation should be done without waiting too long in the severe case.

Section of Anæsthetics

President—A. D. Marston, D.A.

[*February* 6, 1942]

Resuscitation

By Geoffrey Organe, M.A., M.D., D.A.

Causes of Death on the Table

Ultimately, death is due to heart failure, which may be primary or secondary.

Primary heart failure may be due to sudden stopping of the heart or to ventricular fibrillation. It occurs, most commonly, during light anæsthesia, either during induction or shortly after the start of the operation. Heart failure due, solely, to an overdose of anæsthetic probably does not occur; the dose of ether required to stop the heart is nearly half as much again as the dose which stops respiration. Chloroform anæsthesia, uncomplicated by operative stimuli, may be taken down to respiratory failure, when the heart will continue to beat until the effects of anoxæmia are felt (Meek, 1941).

Sudden stopping of the heart is probably due to vagal inhibition excited reflexly from the respiratory tract or from a painful stimulus elsewhere. It may be initiated, for instance, by the application of concentrated chloroform vapour to the nasal mucous membrane. It is often associated with the presence of lymphatic hyperplasia—I dare not say status lymphaticus! The heart itself may be entirely healthy and will resume its normal rhythm on the application of a suitable stimulus.

Ventricular fibrillation, which appears to be the commoner condition, is usually set off by the same stimulus, but it seems to depend on the presence of an abnormally irritable myocardium. Vagal inhibition of the normal pacemaker, here releases lower ectopic foci of irritability which set off the irregular contractions. Among anæsthetics, cyclopropane and chloroform are the chief offenders; yet sudden death during induction with cyclopropane (that is, without operative stimuli) is comparatively rare, probably because the stimulus provided by chloroform vapour is lacking. It is the present fashion to regard all cases of sudden heart failure as due to fibrillation—a point obviously rarely capable of verification in human beings. Guedel (1937) quotes, as such, three cases of heart failure under light ether anæsthesia. There is no conclusive evidence that ether does appreciably sensitize the myocardium, and it seems more likely that these were instances of cardiac standstill. On the basis of available writings, I question whether ventricular fibrillation occurs under ether anæsthesia except when large amounts of adrenaline have been injected by the surgeon. The role of adrenaline in these cases is not quite clear. Nobel and Rothberger (Meek, 1941) thought it stimulated the vagus, inhibiting the upper centres, and allowing the escape of lower foci in the auricles and ventricles; in large doses, certainly, it also directly stimulates the ventricles. The lower centres, not normally being under any vagal control, respond with a few scattered beats which can rapidly increase, developing into a multifocal ventricular tachycardia and finally ventricular fibrillation. The protective action against adrenaline of atropine, or of cutting the vagi, eliminates the vagal inhibition. The sinus node is accelerated and, to become dominant, the ventricular automatic centres have to be stimulated to a much higher degree if ventricular tachycardia is to develop. Nathanson, quoted by Meek, induced cardiac standstill in the human being and then produced automaticity in the lower centres by an injection of adrenaline. This was attributed to a direct action of adrenaline on the heart muscle.

From all this emerges the fact that optimal conditions for the production of ventricular fibrillation arise with the injection into the ventricle of adrenaline when the heart has stopped.

Substances which decrease heart excitability eliminate the adrenaline effect; such are quinine and quinidine orally (Bardier and Stillmunkes, 1922, 1926), and procaine (Shen and Simon, 1938) and cocaine (Hermann and Jourdan, 1931) intravenously. Burstein and others (1940) reported some remarkable instances of recovery in dogs after the intracardiac injection of procaine, 5-10 mg. per kilo, in 5 c.c. of normal saline.

Secondary heart failure is due to anoxia of the myocardium; failure occurs earlier with ethyl chloride or chloroform owing to the toxic effect of the anæsthetic, which is directly proportional to the dose.

Anoxia of the heart muscle may be part of a generalized anoxæmia due to respira-

tory failure or obstruction, or to breathing an atmosphere deficient in oxygen; it may be due to anæmia; it may be due to a deficient coronary circulation resulting from peripheral circulatory failure. Anoxæmia plays, also, a secondary part in increasing the tendency to cardiac irregularities leading to fibrillation.

Treatment

The treatment may be discussed as preventive and restorative. Preventive treatment, apart from the avoidance of grosser errors, is of little effect in primary heart failure; restorative measures are likely to be ineffective in secondary heart failure.

Preventive treatment in secondary heart failure.—The main indications in the prevention of secondary heart failure are for the maintenance of (*a*) blood-pressure, of (*b*) an adequate volume of circulating blood, and, of course, of (*c*) an adequate supply of oxygen.

(*a*) *Blood-pressure*: It seems reasonable, where blood-pressure fall is due to peripheral vasodilatation, as in spinal anæsthesia, to use a drug which will constrict the blood-vessels. The most widely used is ephedrine, which gives good results; neosynephrine, of which I have no personal experience, may be better—of all the sympatheticomimetic drugs it is the least likely to produce cardiac irregularities. Both are very closely related, chemically, to adrenaline. Neosynephrine is less active than ephedrine and its effect is relatively transient, but it may be repeated without loss of efficiency and has been found effective where ephedrine had failed (Lorhan and Lalich, 1940, Bittrich, 1939); the recommended dose after a fall in blood-pressure is one or two minims of a 1% solution, intravenously, repeated as necessary. Prophylactically, not more than one grain of ephedrine should be given intramuscularly; with larger doses the blood-pressure often rises to 40-50 mm.Hg above the normal. To combat an already established fall in blood-pressure, ephedrine, gr. ¼ to ½, may be injected into a vein. The recovery is dramatic and is fully established in one or two minutes; it is better to repeat small doses than to risk the development of cardiac complications by an overdose. It is probably unwise to allow the systolic blood-pressure to fall below 80 mm.Hg.

(*b*) *Blood volume*: Lack of an adequate volume of circulating blood is the basic factor in the production of what we call shock and, in that condition, is accompanied by an increased permeability of the capillary walls, allowing leakage of plasma into the tissues; this is aggravated by anoxia. The normal reaction to fall in blood-pressure due to hæmorrhage or similar cause is peripheral vasoconstriction which is present in shock; the use, here, of a vasoconstricting drug still further reduces the supply of oxygenated blood to the capillaries and produces, ultimately, a deterioration rather than an improvement.

Cold and fear are important contributory factors which will require attention.

You will remember that chloroform and ether increase capillary permeability. The use of ether intravenously was discarded nearly thirty years ago, except as a museum piece, on account of the frequent occurrence of grave complications resulting directly from this. Magnus (Marx, 1931) failed to produce œdema with large saline infusions in normal rabbits unless they had been anæsthetized with chloroform, ether or chloral hydrate. It seems clear, on the evidence at present available, that ether and chloroform are to be avoided, except in minimal quantities, where the patient's condition gives rise to anxiety.

Restoration of the blood volume will, if the shock is not too firmly established, result in vasodilatation and a more efficient circulation. Quite a severe degree of anæmia can be tolerated provided the blood volume is adequate; this accounts, in part, for the greater severity of symptoms resulting from acute than from chronic anæmia.

The indication is for the intravenous administration of fluids. Grant (1942) suggests that a neglected systolic blood-pressure of 80 mm.Hg or less may result in the development of that condition of intense vasospasm in which introduction of fluids is difficult and response is poor. We may therefore take as our standard, requiring correction, a systolic blood-pressure of 90 mm.Hg or less, and aim to maintain it at a little over 100 mm.Hg.

Hypodermoclysis is clearly useless in a condition where fluid is being lost from the blood into the tissues. Intravenous saline has an immediate stimulating effect and, in a mild case, may succeed in breaking the vicious circle. Usually, serum or plasma will be necessary; blood is indicated where hæmorrhage has been severe or where anæmia was present before operation; in shock with hæmoconcentration it is clearly unnecessary and even undesirable. There seems to be no limit to the amount that can be given. Grant used from two to thirteen pints of blood (the last in the space of twenty-eight hours). The first pint or even more may be run into the vein as fast as possible (usually taking five minutes). The amount of blood given should be limited to the

estimated amount lost, further fluid required, as indicated by the blood-pressure, being made up with serum or plasma, or even saline. We are now told that the renal failure sometimes ensuing is due to the crush syndrome and has nothing to do with the quantity of blood given.

The use of so-called cardiac stimulants in a patient gravely ill from shock or hæmorrhage may be dangerous.

CASE I.—A man, aged 52, was gravely ill from hæmorrhage during a perineo-abdominal excision of the rectum, the blood-pressure being unrecordable. Coramine, 1·7 c.c., was injected intravenously, whereupon he died, anticipating the natural course of events, probably by ten or fifteen minutes.

(*c*) *Oxygen supply*: The supply of oxygen to the blood may be reduced by respiratory obstruction; by an inadequate proportion of oxygen in the anæsthetic mixture; by deficient pulmonary ventilation; by impaired gaseous exchange (as after poison gas). In all these, cyanosis will be present and the remedy clear.

The question arises of giving large proportions of oxygen to patients with a diminished oxygen-carrying capacity of the blood. With normal pulmonary ventilation, negligible improvement is produced by increasing the oxygen above 30%. Where breathing is also depressed, as is often the case, higher proportions of oxygen will mask the deficiency. It is questionable whether it is not better to rely mainly on increasing the respiratory movement, incidentally assisting the circulation. This may be done by some form of artificial respiration or by using carefully controlled amounts of carbon dioxide, not exceeding 5%.

Where the respiratory centre remains depressed in the presence of adequate oxygenation, a respiratory stimulant may be considered. For this purpose, picrotoxin, 3 mg., cardiazol, ½-1 c.c., coramine, 1-2 c.c., or alpha-lobeline, intravenously, are suitable. Intravenous injection is, to my mind, preferable; the dose may be divided and the effect exactly judged. The dose required is less than may be use in barbiturate narcosis for its analeptic effect and should be no larger than is needed, lest a secondary depressant effect come into play. It should be borne in mind that the usual analeptic dose of coramine—5 c.c.—is the same as that used for the production of convulsions in the treatment of schizophrenia.

Clearly, in the gassed patient, with impaired gaseous exchange in the lungs, the oxygen percentage must be as high as possible. I can think of no anæsthetic as suitable as cyclopropane.

As both lowered blood-pressure and oxygen lack enhance the depressant effects of anæsthesia, an essential part in the treatment of a patient whose condition shows deterioration consists of the withdrawal of the anæsthetic. If avertin or a barbiturate is playing any considerable part in the anæsthesia, an analeptic dose of cardiazol or coramine should be given intravenously—sufficient to produce the desired result.

Preventive Treatment of Sudden Heart Failure

The preventive treatment of primary heart failure consists of pre-operative atropine or scopolamine to inhibit the vagus; the avoidance of the chief culprit—chloroform; avoidance of excitement during induction of anæsthesia and of premature operative stimuli; exceeding caution in the use of adrenaline—absolutely contra-indicated with chloroform or cyclopropane.

The direct protective action of barbiturates against untoward effects from adrenaline has lately been questioned (Orth *et al.*, 1941). Their value in by-passing the second stage of anæsthesia is obvious.

Restorative treatment in primary heart failure.—Established methods: Many textbooks of surgery confine themselves to the statement that cardiac massage through the diaphragm has been found of value; others suggest the intraventricular injection of adrenaline, ♏ 10, ether, ♏ 20, pituitrin, ½ c.c. Hewer (1939) mentions also strophanthus, digitalis, camphor, coramine, strychnine and dextrose, pointing out that their diversity of action suggests strongly that it is the mechanical stimulus of the injection that is responsible for the restoration of the heart beat; to this stimulus the auricle is much more sensitive than the ventricle.

Drugs.—Intravenous, intramuscular or subcutaneous injections are clearly useless without a circulation. For intracardiac injection, the drugs most commonly in use are adrenaline and coramine. Coramine has no direct action on the heart and is not indicated.

Gunn and Martin (1915) found, in dogs, where twenty minutes of direct cardiac massage had failed, that intrapericardial injection of adrenaline restored the heart beat almost at once. It was unsuccessful alone. We know that adrenaline can initiate ventricular fibrillation under chloroform and, in sufficiently large doses, under ether. As it acts directly on the ventricles it seems reasonable to suppose that the intraventricular injection of the usual dose (1 : 1,000 solution, 10-15 ♏) may produce fibrillation with ether, especially where the tendency to irregularities has been enhanced by a period of anoxia. Tournade and others (1932) reported recovery from chloroform syncope in the dog by intravenous or intracardiac injection of adrenaline combined with massage and artificial respiration. Meek comments "these must have been a simple toxic depression of the heart, a real chloroform syncope". One in ten of these developed fibrillation.

The following case illustrated the inadequacy of accepted methods of resuscitation:

CASE II.—A boy, aged 13, was anæsthetized by a house surgeon for bilateral inguinal herniorrhaphy. Premedication was omnopon gr. $\frac{1}{3}$ and scopolamine gr. $\frac{1}{150}$ (far too large a dose) two hours beforehand. The anæsthetic was open ether, preceded by ethyl chloride, and the course was at first uneventful. Shortly after the incision on the second side, under what was said to be deep anæsthesia, he *suddenly* stopped breathing, was pulseless and apparently dead. Adrenaline, 1 : 1,000, ♏ 10 was injected into a ventricle. On attempting cardiac massage through an abdominal wound, the surgeon found what he described as irregular, feeble contractions—evidently ventricular fibrillation. The lungs were then inflated at regular intervals with oxygen under pressure. Regular, very forcible heart beats started and his colour returned. The pupils were $\frac{3}{4}$ dilated. After ten minutes of artificial respiration by compressing a closed re-breathing bag, occasionally emptying and refilling with oxygen, breathing recommenced. He was returned to the ward in about twenty-five minutes, breathing quietly and with pupils half dilated. The pulse was slower and the heart beat less exaggerated.

[Two hours later, twitching was noticed in the arms and legs. In the next four hours he had several generalized fits. It was found that he had had continuous intranasal oxygen with carbon dioxide, which was at once stopped; there were no more generalized fits. Five hours later he was less deeply comatose and definitely irritable, responding to manipulations by whimpering and mild convulsive movements, mainly in the limbs, especially the arms, but also in the face. The oral airway was removed with the aid of a gag, and he became quieter. The plantar reflexes were extensor. The patellar, biceps and triceps jerks were uniformly increased. During the fits, the eyes were turned upwards, with nystagmoid movements. His temperature was 103° F. Tepid sponging was ordered and a rectal drip saline started. Three hours later he was more spastic and his legs were crossed at the thighs.]

He died in twenty-three hours after operation, cyanosed, with a temperature of 106° F.

At post-mortem the thymus was found markedly increased, with generalized lymphatic hyperplasia. There were the usual signs of an asphyxial death.

The period of circulatory arrest was about five minutes.

The history of the case and the presence of status lymphaticus suggest to me that the heart stopped from vagal inhibition. It is my opinion that the fibrillation was induced by the injection of adrenaline, and that cardiac massage, first, might have had a more favourable result.

Mechanical stimuli.—Lowering the head of the table is widely practised and may be successful in reviving the patient. Artificial respiration alone may be sufficient to restore the heart. Auricular puncture, if done before the irritability of the auricles has been lost from anoxia, is an adequate stimulus.

CASE III.—Some years ago I anæsthetized a girl, aged 17, for tonsillectomy. The surgeon liked chloroform and, as he had given many more anæsthetics than I had myself, I was not disposed to argue. She had atropine, gr. $\frac{1}{75}$. I induced anæsthesia with ethyl chloride and chloroform-ether mixture to the third plane of the third stage and took her into the theatre, where she had chloroform and oxygen through a Davis gag. Shortly after the surgeon had begun I noticed that she was not breathing; she was pulseless and I could not hear the heart. The auricle was pierced with a handy lumbar puncture needle; to my relief I saw it ticking to and fro, the pulse had returned, and breathing started spontaneously. The operation was completed with oxygen and ether, and all was well.

CASE IV.—A healthy man of 52 became obstructed, under pentothal anæsthesia, by an intense laryngeal spasm which I could not overcome with artificial respiration. His face, which was cyanosed, became blotchy white, intra-ocular tension dropped and there was no sign of a heart beat. Immediate auricular puncture restored the heart. Intermittent inflation of his lungs through an oral endotracheal tube restored his

colour, and the pulse gradually returned. The operation—removal of a malignant ulcer of the tongue by diathermy cautery—was completed with nitrous oxide and oxygen. Respiration was still rather depressed at the end but was satisfactorily stimulated by intravenous injection of 2½ c.c. of coramine. He was well the next day.

Ventricular puncture without injection is ineffectual.

Cardiac massage through the intact abdominal wall is a waste of valuable time in adults. Massage through the intact diaphragm, though less effective than direct massage, involves less drastic surgery and is often adequate. Ogilvie (1929) states that only direct massage can maintain the circulation artificially. In one case of his there was no spontaneous heart beat for seventy-five minutes, though the patient remained a good colour, and was breathing, groaning and moving spontaneously.

Gunn and Martin suggest that massage should be carried out at less than half the normal rate to allow filling which, in the absence of auricular contractions, is entirely passive. Compression should be gradual to avoid injury, and relaxation rapid. They say that continuous massage, while helping the circulation and the elimination of anæsthetic, may cause feeble spontaneous beats to disappear again. This may have happened in Ogilvie's case. There should, therefore, be pauses as soon as even feeble beats have begun.

Irritability to mechanical stimuli is soon lost and speed is the essence of the matter.

Where irritability is so far lost that no response is found to direct massage, the violent stimulus of intraventricular adrenaline may still produce results. Massage should be resumed as soon as the injection is completed.

I am indebted to Dr. Nosworthy for an account of the following case:

CASE V.—A soldier, aged 25, was wounded in the chest at point-blank range by a single machine-gun bullet, entering between the 5th and 6th ribs near the sternum. The wound was excised at the C.C.S. On arrival at the Base his general condition was poor, pulse 120, with right hæmothorax. He developed bronchopneumonia on the opposite side and was dyspnœic, with a pulse of 130. A further exploration was undertaken three days after the injury.

Anæsthesia: endotracheal cyclopropane and oxygen with bronchial suction. There was a hæmatoma of the mediastinum and right hilar region. The damaged upper and middle lobes were removed by tourniquet.

Suddenly, while suturing the hilum, the heart stopped and his colour rapidly deteriorated. The heart was massaged with difficulty through the mediastinum for eight minutes without response. Adrenaline was injected, with almost immediate effect; at the end of twelve minutes the heart was beating satisfactorily. He took a deep breath and the colour flooded back to his face. The operation was completed without further anæsthetic.

At the end of the operation the temperature was 105° F. Left on oxygen, he recovered to the stage of eye movements, but he had gasping respirations. There was no further improvement in two hours and he died within a minute of withdrawal of oxygen. His temperature was 106° F.

Post-mortem findings: Bronchopneumonia of the left lower lobe. Œdema and asphyxial signs in the brain.

Treatment of the resuscitated patient.—After even a short period of cardiac arrest, there is usually a degree of general, but especially of central nervous system depression.

Cortical depression is marked by prolonged coma which, though causative of anxiety, does not require treatment. Any remaining stages of the operation can be completed with little or no anæsthetic. Medullary depression shows itself by a lowered blood-pressure and, more important, by apnœa. It may be necessary to keep up artificial respiration for some little time, seeking relief by cautious injection of respiratory stimulants already mentioned. The patient must be carefully watched until recovery is complete, as any minor accident might prove fatal. Intravenous glucose saline may usefully be given as a circulatory stimulant.

Suggested Routine for Resuscitation

I suggest the following routine measures for resuscitation after sudden heart failure, which differ in one or two important respects from the procedure accepted generally among surgeons.

(1) Clearing of the airway and establishment of artificial respiration with oxygen. Sylvester's method may be used, rhythmical inflation with oxygen from a suitable machine, or rhythmical compression of a closed re-breathing bag. Care must be taken when an endotracheal tube is in use; I have seen, at post-mortem, widespread surgical emphysema from rupture of the lung due to over-enthusiastic insufflation of oxygen.

Insufflation of oxygen through a narrow-bore endotracheal tube is not recommended; the movements of respiration are of valuable assistance in re-establishment of the circulation.

(2) As soon as artificial respiration has been established, auricular puncture should be made with any available needle of 3½ in. or more in length—Hewer's cardiac puncture needle or a lumbar puncture needle—piercing the chest wall in the third right intercostal space ½ in. from the sternum and passing inwards and towards the mid-line. The risks attendant on this are small compared with those of delay.

(3) Should auricular puncture fail to produce an *immediate* response, cardiac massage must be started through an upper abdominal incision, sterility being secondary to the necessity for speed.

(4) If massage through the diaphragm is not effective within four minutes of the onset of heart failure, a 3 in. incision must be made in the diaphragm and an artificial circulation established by direct massage at a rate of forty compressions a minute.

(5) If a satisfactory artificial circulation is not established, or if spontaneous beats have not appeared in ten minutes, then, and only then, adrenaline 1 : 1,000, ♏ 10, may be injected into the ventricle through the fourth left intercostal space two inches from the border of the sternum, as a measure of desperation.

(6) It seems a justifiable risk, if the surgeon's hand confirms ventricular fibrillation, to inject into the cavity of the left ventricle 10 c.c. of 2% procaine.

If a satisfactory circulation is not established within four or five minutes, permanent damage to the brain is likely to occur, leading to death at a later period, as in Case II.

REFERENCES

BARDIER and STILLMUNKES (1922), *Arch. internat. de pharmacodyn. et de thérap.*, **27**, 375.

Id. (1926), *Compt. rend. Soc. de biol.*, **94**, 1063.

BITTRICH, N. B. (1939), *Anesth. & Analg.*, **18**, 29.

BURSTEIN, C. L., MARANGONI, B. A., DE GRAFF, A. C., and ROVENSTINE, E. A. (1940), *Anesthesiology*, **1**, 167.

GRANT, R. T. (1942), *Proc. Roy. Soc. Med.*, **35**, 445.

GUEDEL, A. E. (1937), "Inhalation Anæsthesia", 85. New York.

GUNN, J. A., and MARTIN, P. A. (1915), *J. Pharmacol. & Exper. Therap.*, **7**, 31.

HERMANN & JOURDAN (1931), *Compt. rend. Soc. de biol.*, **106**, 1153.

HEWER, C. L. (1939), "Recent Advances in Anæsthesia and Analgesia". 198, 3rd Ed. London.

LORHAN, P. H., and LALICH, J. J. (1940), *Anesth. & Analg.*, **19**, 66.

MAGNUS, R. (1899), *Arch. f. exper. Path. u. Pharmakol.*, **42**, 250.

MARX, H. (1931), *J. Pharmacol. & Exper. Therap.*, **41**, 483.

MEEK, W. J. (1941), *Physiol. Rev.*, **21**, 324.

NOSWORTHY, M. D. (1942), Personal Communication.

OGILVIE, W. H. (1929), "Recent Advances in Surgery", 147. 2nd Ed. London.

ORTH, O. S., WANGEMAN, C. P., and MEEK, W. J. (1941), *Anesthesiology*, **2**, 628.

SHEN and SIMON (1938), *Arch. internat. de pharmacodyn. et de thérap.*, **59**, 68.

TOURNADE, MALMEJAC, and DJOURNO (1932), *Compt. rend. Soc. de biol.*, **110**, 540.

JOINT DISCUSSION No. 3

Sections of Medicine and Surgery

Chairman—GEOFFREY MARSHALL, O.B.E., M.D.
(President of the Section of Medicine)

[*January* 27, 1942]

DISCUSSION ON METHODS OF RESUSCITATION IN SHOCK

Dr. R. T. Grant: In comparing the efficacy of different methods we are at once in difficulties because of the confusion in the definition of the word "shock" even when qualified by the adjective "traumatic". In practice there is a wide variation in the application of the term. Some medical officers apply the label "shocked" to any patient, however slightly wounded, who seems ill, is pale and has a weak pulse. Others restrict it to cases displaying low blood-pressure, a rapid thready pulse, pallor and cyanosis, a cold and sweating skin, shallow rapid respirations and often vomiting, restlessness, a lessened sensibility and a dulled mental state. To the majority, the criteria of "shock" are severe injury and low blood-pressure. The lack of a common basis of diagnosis renders it difficult to assess the efficacy of the various methods of treatment adopted. In dealing with air-raid casualties our first job is to pick out the cases which are seriously ill, our second is to recognize those who are likely soon to become seriously ill if left without rapid treatment. We have then to decide on the remedies to be adopted and later to decide when the patient is fit to undergo surgical operation. This sorting of the patients is determined by the nature and extent of their injuries, by the amount of blood lost and, lastly, by the state of the circulation as judged chiefly, but not only, by the level of blood-pressure. The remedies available are the simple measures of rest, warmth and the head-down position, drugs such as morphia, adrenaline and pituitrin, oxygen, the giving of fluids by mouth and rectum, and, finally, the intravenous administration of blood or blood substitutes.

Only too often we are uncertain whether the patient has lost much blood or little; only too often we can merely guess as to the nature and extent of his injuries and what part nervous influences are playing in his collapsed state.

In cases of serious injury with severe loss of blood the simple restorative measures, while they may bring about a temporary improvement, are usually insufficient for recovery. Where there are severe injuries and possibly severe blood loss, transfusion should be begun at an early stage. This does not mean, however, that the simpler measures should be neglected, for they are of value even in serious cases. In milder cases they may be all that is required.

The term rest does not imply that the patient should be kept still. It means making him feel comfortable by transferring him as soon as possible from stretcher to warm bed, removing his clothes, examining his wounds as quickly and as smoothly as the circumstances allow, allaying his fears and his pain, and attending to his wants. I stress these points, for they are often neglected. To allay pain, fear, or apprehension, morphia is specially useful. It is given almost as a routine, and we have not seen bad results follow the injection of ¼ gr. We have seen instances in which the giving of morphia has been followed by the subsidence of a raised blood-pressure to normal levels, and others in which a low pressure has risen to normal levels coincident with the relief of pain. It should be remembered, however, that the drug is not well tolerated by some patients and that it may induce or aggravate nausea or vomiting. When the peripheral circulation is greatly reduced, as it often is in these cases, a subcutaneous injection may be but slowly absorbed. A first subcutaneous injection, producing no effect, is followed by a second. If the peripheral circulation meanwhile speeds up, the morphia is more rapidly absorbed. We have seen at least one instance of what we took to be morphia poisoning, probably due to this factor. It should not be forgotten that there are other remedies that may be usefully employed, such as chloral and the bromides by mouth and rectum.

Warmth is also useful in promoting comfort, but heat must be applied with care and moderation. The patient must be watched and the heating reduced or withdrawn when he begins to feel warm. I doubt if it is wise to attempt a rapid warming of the patient and it is certainly not good to leave a cradle on with all its lamps alight for

hours as I have seen done, as the patient becomes uncomfortably hot and restless and sweats profusely.

The raising of the foot of the bed is a measure always worth trying in cases where the blood-pressure is low. It is often followed by a more or less rapid rise of blood-pressure and a general improvement in the patient's condition, which, however, is often not maintained. Sometimes the simple measure of raising the end of the bed leads to a remarkably rapid recovery.

In the severely injured patients these measures are usually insufficient to effect lasting improvement, and transfusion is required. Of the 100 cases which Dr. Reeve and I reported recently only 17 did not receive transfusion; none of these was suspected of having lost much blood and in the majority the injuries were not regarded as severe. Moreover, I think that in several of them transfusion ought to have been given and would probably have hastened their recovery.

In assessing the need for transfusion I would place emphasis on the severity of the injury and blood loss rather than on blood-pressure. In severely wounded cases, therefore, with evidence of blood loss, transfusion should be begun without delay, no matter what the blood-pressure is, low, normal, or raised. It must be remembered that a normal blood-pressure and pulse-rate and even a good facial colour are compatible not only with severe injury but also with much loss of blood. Such cases are not uncommon—there were 10 such in the group of 28 with normal blood-pressure in our series. It should also be remembered that low blood-pressure, pallor, sweating, nausea, and other signs of collapse are not necessarily associated with severe injury or blood loss, and that not all cases displaying these signs require transfusion; they may recover well and rapidly without it.

When there is doubt about the amount of blood loss I think it is better to err on the side of giving transfusion than of withholding it. I have never seen a pint or two of blood or plasma do harm, but on the other hand I have seen collapse occur at operation that would in all probability have been prevented by previous transfusion.

I have no experience of transfusion fluids other than blood and plasma. If choice of these two is not restricted by supply, I use blood rather than plasma because hæmorrhage seems to play such a large part in producing the depressed state of our patients. Of the 63 cases with low blood-pressure in our series, at least 45, or 85%, were judged to have lost much blood. With small transfusion, not more than 1 or 2 pints, I do not think it matters much whether blood or plasma is used but with larger transfusions more blood than plasma should be given. In any case it is well to observe the changes in the patient's hæmoglobin resulting from transfusion, for it does not seem wise to allow the hæmoglobin level to fall below 50%. It is to be remembered that we have not only to restore blood volume but also to ensure an adequate supply of oxygen to damaged and infected tissues. I have in mind an instance where the femoral artery was cut, and the foot though not entirely devoid of collateral circulation became gangrenous. I think it likely that the loss of the foot can be attributed to the low hæmoglobin content of the blood, which for days remained about 45%.

The amount required for resuscitation varies so greatly in different patients that no definite ruling can be given on this point. Of the 83 cases in our series 23 received 2 pints or less, 29 from 2 to 4 pints, 18 from 4 to 6 pints, and 13 more than 6 pints. The largest amount was 13 pints given over a period of twenty-eight hours, and this was called for because of continued bleeding. In general the amounts are related to the degree of blood loss, the larger transfusion being given mainly where bleeding was renewed either before or at operation. But as a guide we may say that restoration and maintenance of normal systolic blood-pressure (100 mm.Hg and over) can be taken as the chief indication that an adequate amount has been transfused. If there is doubt about how much fluid should be given it is a good plan, if improvement has begun and continues, to cut down the rate of transfusion to see if improvement is maintained.

As regards the rate of transfusion, we have found that for early transfusions a rate of 1 pint in a quarter to half an hour is satisfactory, and for later transfusions a slower rate suffices—one pint over one or more hours, except in instances where these later transfusions are required to compensate for renewed bleeding. It is to be remembered that in some cases when the veins are tightly constricted the transfusion fluid will not run freely into the veins and must be given under pressure, either by means of a bulb attached to the bottle, or by a two-way syringe.

More rapid transfusions have been given, apparently with good effect; for example, in one case two pints were administered in nineteen minutes with general improvement and a rise of blood-pressure from 40/20 to 130/70 mm.Hg. But the rise of pressure accompanying a rapid transfusion is not always maintained, whereas with a slower injection of fluid the rise of blood-pressure is more gradual, but is sustained. Further,

rapid transfusion is not always well tolerated; in one case restlessness developed during the transfusion of one pint of plasma in five minutes, and one pint of blood in eight minutes; in two others restlessness and increased rate and depth of respiration were noted to come and go with the speeding and slowing of the transfusion. On the other hand a slow transfusion may be ineffective, the blood-pressure remaining low or continuing to fall until the rate is increased.

In most cases improvement is pronounced within a few hours of beginning transfusion, being shown by a lessening of pallor (sometimes restoration of a good colour), the cessation of sweating, a feeling of warmth, and a rise of blood-pressure to over 100 mm.Hg; slow pulses tend to increase and rapid ones to fall towards normal rates. In some the improvement is dramatic in its rapidity. In a few the response is slow; thus in one instance transfusion of two pints of plasma in the early stages raised the systolic blood-pressure from 50 to 90 mm. but no further, though recovery took place later. This case also illustrates that one factor which slows improvement is delay in beginning transfusion. The patient was not admitted to hospital until five and half hours after injury; transfusion was begun seven and a quarter hours after injury. Blood-pressure was not established at normal levels until some time after operation—about thirty-nine hours after injury.

As a general rule, in the absence of continued bleeding, if no material improvement takes place after giving two or three pints of blood or plasma at an adequate rate, later improvement is unlikely. Amongst our series there were only 6 patients who failed to respond after transfusion of amounts varying from two to six pints and all soon died; in 3 bleeding was uncontrollable; this factor was not evident in the 3 others.

According to our experience, operation should be carried out as soon as possible after the patient is revived. At operation as little as possible should be done as quickly as possible, and blood loss must be kept minimal. The patient requires to be watched for signs of collapse, and transfusion ought to be continued at drip rate during operation so that at any time it can be speeded up to compensate for further hæmorrhage.

Mr. R. Vaughan Hudson: The experience of major surgery in peace time demonstrated that the use of posture, avoidance of movement, warmth, relief of pain and fluids by mouth, although of greatest value, were not always in themselves sufficient to combat shock, or to prevent its occurrence. On searching for additional aids, it was soon found that intravenous salines were of temporary value only, and it was not until whole blood was used that definite improvement occurred.

The first method in order of time was the Kimpton tube, then the Keynes flask, and later the Marriott-Kekwick continuous drip whole blood transfusion. The marked venospasm in established shock was well known to us, and the needle method was early abandoned for the more certain method of the tied-in cannula.

The anæsthetist has played his part. The occurrence of shock on the operating table was manifested to him as a result of trauma, and he noticed a change in colour, a change in respiratory rate and a fall in body temperature. Later the interest and energy of the anæsthetist, making use of continuous blood-pressure readings, demonstrated that the progressive change in shock was the fall in blood-pressure preceding or associated with a rise in the pulse-rate. This use of the blood-pressure apparatus enabled us early to combat shock soon after its commencement, but in fact the surgeon was still waiting for shock to occur before he treated it.

Thus the results did not markedly improve until an attempt was made to anticipate shock, so that the employment of posture, avoidance of movement and use of warmth, were supplemented by whole blood transfusion, commenced in the anæsthetic room, maintained during the operation and post-operatively. In the road casualty these methods were employed as soon as the patient was admitted to the ward, in order to control and combat shock.

Provided that surgical technique was correct and infection avoided, recovery was satisfactory, and major surgery was made possible without primary or secondary shock; but after a varying post-operative time interval, conditions mimicking so-called secondary shock were produced in cases complicated by the non-closure of large exposed areas, or by infection. In these cases death occurred in a manner which was similar to shock and from circulatory failure produced again by a factor derived from the site of the wound.

The military surgeon deals with the healthy and strong but the civilian surgeon faces trauma inflicted upon the normal and also upon those burdened by constitutional disturbances, such as diabetes and cardiovascular disease. That the close-co-operation between physician and surgeon should be maintained in war as in peace is self-evident. War no less than peace has demonstrated again and again that the apparently weak may survive the identical injury which kills his healthy fellow—this encourages the attendant not to give up his strivings, because the apparently hopeless case will, and does, survive.

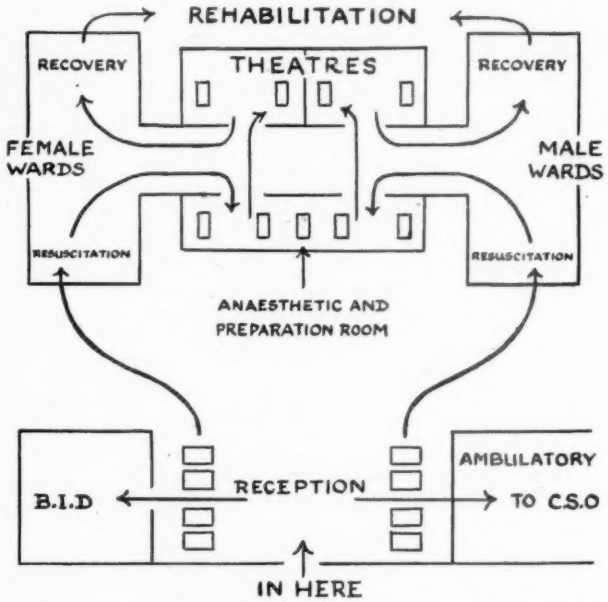
The civilian war casualty has added two main items which were not seen in peace time:

the incredible dirtiness of the casualty due to debris, and the condition known as "blast", the effect of which depends upon the proximity of the patient to the explosion. As a consequence the casualty exhibits a degree of shock which is more profound than that seen in peace time, because the total area of injury is greater although its severity is not necessarily evident upon the surface, but concealed within the ruptured deeper tissues.

Certain general conclusions based upon experience and reasonable conjecture may be drawn as a working basis. Shock inevitably accompanies an injury, it is the expression of an injury, the response to injury, the injury being the causative agent. The fundamental changes are manifested by the cortical centres and the vegetative nervous system.

The cortex expresses either undue exaltation, or confusion and depression, either of which may accompany the changes in what may be termed the automatic nervous system, which in its turn exhibits a prodromal, an intermediate, and a conclusive phase.

These phases may succeed one another with appalling rapidity. In the prodromal period the compensatory mechanism of the nervous system exhibits its conservatism by a slow pulse and normal blood-pressure. This is the dangerous period, and is frequently



Organization and method of dealing with air-raid casualties at the Middlesex Hospital.
[B.I.D. = Brought in dead. C.S.O. = Casualty Surgical Officer.]

ignored or unrecognized. The intermediate stage is the early failure of the compensatory mechanism, in which the pulse may be slow, but the blood-pressure falling. This stage is the inauguration of circulatory failure. In the conclusive stage the mechanism has failed, the pulse-rate is rising, the blood-pressure low and circulatory failure established.

Shock, therefore, appears to be a disturbance of the circulatory mechanism.

Clinically all these phases are accompanied by coldness, pallor of the whole body, peripheral spasm of arteries and veins, and tonelessness of the tissues.

Recovery passes through these phases, but in the reverse order, though the pulse-rate may still be raised in spite of the fact that the blood-pressure is within normal limits. This condition of shock can be mimicked by any cause of circulatory failure, originating in the cortical mechanism, the vegetative mechanism or organic lesions of the circulatory mechanism itself.

The diagnosis rests upon the clinical signs and aid of the blood-pressure apparatus.

The treatment is directed to the mechanism of the patient as a whole, and the nature of the injury.

Although whole blood is considered by us to be the best anti-shock measure, we have relegated its use in war time to exsanguinated patients and employed the more practical plasma, and, in a few cases, serum. These substitutes have been highly efficacious.

The treatment of the wound is of urgency to prevent and control infection. By the removal of dead and dying tissue and their products, by relieving hypertension and correcting hypotension of the damaged tissue, by immobilization of, or resting the injured area, we are preventing further injury and minimizing absorption of the products of damaged tissue. In fact we are stabilizing the patient, relieving pain and preventing further shock.

In the past treatment was focused upon the wound and the general condition of the patient ignored, a phase then occurred in which too much attention was paid to the general condition of the patient and the wound relegated to the background. Now we appreciate that both patient and wound must have simultaneous treatment.

Organization and training in reception and dealing with the injured are of the greatest importance. The personnel, the accommodation, the equipment are kept ready for immediate work. All concerned understand the definite plan, where the equipment is kept and how to use it.

In the Resuscitation Ward a plasma drip is put up on all patients with wounds. In addition it is put up on all those who are considered to be likely to need or benefit by it. Its rate and its quantity is controlled by the blood-pressure reading. As soon as possible the patient is stripped and examined from head to foot and his theatre priority denoted.

In the Anæsthetic Room all preparation of the skin is performed under gas and oxygen anæsthesia preceded by a minimal dose of pentothal injected into the "drip" tubing.

In the theatre foreign bodies are removed and the wound widely decompressed, but dead and dying tissues are sparingly removed.

In glass wounds primary suture is often possible but irregular wounds caused by foreign bodies are left open and packed lightly with vaseline gauze and sulphanilamide.

Wherever possible plaster slabs are made use of for immobilization.

In the recovery ward the strictest attention is paid to the fluid intake and output with special reference to the urinary flow.

In burns the routine differs little, but we cut down, if necessary, through burnt tissue to establish the plasma drip, and we have found of value the Stannard sheeting and envelopes in the treatment of these cases.

The onus of decision as to operation, resuscitation, transference to the theatre and advice in the theatre, rests with the most experienced surgeon present, who should walk and keep walking, continually collaborating with his fellow physician in order to carry through without delay the treatment of the injured. The value of the help of a physician, particularly in thoracic and cardiovascular problems cannot be over-emphasized.

We believe that the policy of preparation and organization for immediate surgery has benefited our patients. The teams of apprentice surgeons, nurses and dressers have borne the burden of the actual work, loyally supported by lay helpers. The following are the results of these labours:

Of the total cases admitted 4% died without surgical intervention. This small group consisted in the main of the crush syndrome and severe fracture of the skull. Of the remainder, consisting of 96% of all cases admitted, the final mortality was 3·8%.

We have been fortunate to work in a soundly constructed building, which, so far, has not been too severely damaged, although we had to make use of supplementary heating, water and lighting arrangements on more than one occasion.

Dr. J. McMichael: In order to have a satisfactory conception of the type of case which we are attempting to treat, I think it is necessary to try to systematize the facts so patiently collected by Grant and others into some scheme which reveals more clearly the various clinical types of shock. The reactions to injury which we can now recognize are shown in the following table:

CLINICAL TYPES OF "SHOCK".

Effects of injury:
- (1) Fright (emotional "shock").
- (2) Post-traumatic hypertension.
- (3) Neurogenic shock (pulse slow).
  - (*a*) Vasovagal.
  - (*b*) Brain injury.
- (4) Oligæmic shock.
  - (*a*) Blood loss.
  - (*b*) Plasma loss.
  - (*c*) Blood *and* plasma loss.
- (5) Crush syndrome (renal failure).
- (6) Circulatory collapse due to mechanical causes.
  - (*a*) Fat embolism.

Medical factors		(*b*) Pulmonary embolism.
		(*c*) Coronary thrombosis.
	(7)	Toxæmic shock.
		Bacterial toxins: Diffuse peritonitis, &c.
	(8)	Dehydration collapse.
		Gastro-enteritis.
		? diabetic coma, &c.

This table includes a considerable range of conditions, the least severe of which is simple emotional "shock" or collapse associated with nothing more than the distress occasioned by the experience of an accident or bomb incident. It is now well recognized that renal failure may be a remote effect of crushing injury, and it appears that the "condition of lowered vitality due to injury" may result from changes in organs outside the circulatory system. It seems, therefore, that we must admit the wisdom of the definition of shock in the older textbooks as "a condition of depressed vitality due to injury", and we must include under the heading of "The remote effects of injury" such conditions as renal failure. We must also recognize such conditions as *post-traumatic hypertension*, which may be associated with pallor and a rather thin thready pulse; this condition was described by Grant and Reeve in their recent analysis. *Neurogenic shock* includes those cases in which the pulse is slow. This may be a simple vaso-vagal type of faint, although rather prolonged, or it may occur in the more serious condition of brain injury. In either case the treatment consists of rest in a recumbent position. The work of Wallace and Sharpey-Schafer has shown that the vaso-vagal type of collapse is a frequent sequel of hæmorrhage where the blood loss is in the neighbourhood of 1-1·2 litres. Vaso-vagal collapse, therefore, does not exclude the possibility that there may be a considerable reduction of blood volume and these cases have to be very carefully watched. *Oligæmic shock* may result from hæmorrhage, from loss of plasma fluid from the circulation as in burns and crushing injuries, and occasionally these two factors may be combined. Mechanical causes, such as fat embolism, may also complicate the picture.

At the other end of the scale there are the various medical factors which may also produce circulatory collapse, such as massive pulmonary embolism and coronary thrombosis; the latter condition we have seen in an elderly patient who also had oligæmic shock. Presumably the slow blood flow occasioned by blood loss is the factor determining the development of thrombosis on previously diseased coronary arteries. *Toxæmic shock* is a term which we can apply to the collapse which follows sudden flooding of a serous cavity with infected material, as, for example, by a ruptured appendix. *Dehydration* may also play a part in the production of collapse, as, for example, in prolonged diarrhœa or vomiting.

Thus the word "shock" when unqualified has no well-defined meaning, and I suggest that we should always qualify the word in the above manner to indicate clearly the type of case under discussion. The remainder of my remarks will be concerned with the treatment of "oligæmic shock".

I intend to emphasize the more important points in the practical management of cases of wound shock by discussing the mistakes made in the management of some of our earlier cases in the light of advancing knowledge.

A woman of 56 (see *Edinburgh M. J.*, 1941, **48**, 160, fig. 3) was our first air-raid casualty. She had sustained multiple injuries of which the most serious was a compound fracture of both bones of the left leg, by which she had been pinned under a fallen beam for many hours. On admission she was cold and collapsed, blood-pressure being under 70 mm.Hg. A serum transfusion of 1,620 c.c. was given in fifteen minutes, with an excellent immediate result, the blood-pressure rising from 70 to 140 mm.Hg. Speed of transfusion is important. The normal heart pumps four litres of blood per minute at rest, and an extra 100-200 c.c. per minute imposes no appreciable difficulty. In oligæmic shock, therefore, we have confidence in giving transfusions as rapidly as they can be made to run until the blood-pressure is restored to normal; only then should the transfusion be slowed to a drip. In this case a mistake was made in dismantling the apparatus after the blood-pressure had been restored and missing the optimum time for operation. Two hours later the patient had collapsed again, and in spite of further massive transfusion (1,440 c.c.) the blood-pressure response was much less satisfactory. The deleterious effect of delay is thus demonstrated. A further fault was to allow the patient to go to the operating theatre where she was subjected to extensive operative procedures without further transfusion; on return to the ward the pulse was imperceptible, the blood-pressure 40 mm.Hg, and a further blood transfusion could not be given sufficiently rapidly to restore the blood-pressure, which only rose to 80 mm.Hg after 1,620 c.c. blood. After three hours it was apparent that further efforts were useless and the patient died shortly afterwards. It is thus important to realize the *optimum*

time for operation is the earliest moment after restoration of the circulation, the *more prolonged the collapse the more difficult* it may be to get an adequate effect from transfusion alone, and *partial restoration* of the blood-pressure is wholly inadequate to save life. When the blood-pressure has been too low for too long, the circulatory collapse becomes irreversible. There may be difficulty in getting blood to flow when collapse is extreme, as the superficial veins seem to go into spasm. Useful measures in such cases are warming of the limb along the line of the vein and ensuring that the blood is warm as it runs in.

When the blood-pressure is low as a result of oligæmia, the critical level at which transfusion is necessary seems to be about 80-90 mm.Hg. Our belief that this is the critical level is based on records of two cases in which transfusion was given and in which the transfusion was stopped when the blood-pressure had reached 85 or 90 mm. Hg. The cases were left with blood-pressures at this level for four or five hours. Collapse occurred at the end of this time, and in spite of further transfusions, death occurred. In one patient who had had a severe hæmatemesis I measured the cardiac output by the acetylene method when the blood-pressure was 90 mm.Hg. The figure obtained indicated a heart output less than half the normal and therefore the oxygen supply to the tissues in such a case was in serious jeopardy. I regard this level of blood-pressure as dangerous only in cases of oligæmic shock. Where circulatory collapse has resulted from other causes, for example coronary thrombosis, and in many cases of post-operative shock where the condition is complicated by the effect of anæsthetics, recovery can occur perfectly well from blood-pressures which are lower than 80 mm.Hg. The reason for this difference is obviously a matter requiring further research.

A second case (*Edinburgh M. J.*, 1941, **48**, 160, fig. 2) was that of an Army officer who had sustained punctured wounds of an arm and a leg together with a compound fracture. Subsequent operation showed considerable blood loss into the lacerated soft tissues. On admission his blood-pressure was 110 mm.Hg and he was cold. He was warmed under a shock cage with considerable zeal. An hour later he was found to be hot and perspiring, while the blood-pressure had fallen to 70 mm.Hg. He responded well to transfusion which was maintained through the operation, and his subsequent course to recovery was uninterrupted. I think a major error was overheating. It should be remembered that the warm skin holds at least 500 c.c. more blood than the cold, and when blood is scarce in vital organs, overheating is certainly undesirable. Blalock and Mason have recently shown that dogs bled to a blood-pressure of 75 mm.Hg survive about four times as long when cooled as they do when warmed. Results would improve if heating was not carried out with such enthusiasm. Adequate cover for comfort is probably all that is required.

Pulse-rate.—It has been repeatedly stressed that pulse-rate is a poor guide in the assessment of a case. In the instance of a small boy (*Lancet*, 1940 (ii), 774, fig. 9) whose right kidney had been crushed by a lorry wheel, transfusion and restoration of the blood-pressure were accompanied by acceleration of the pulse from 130 to 180 per minute. Two days elapsed before the pulse subsided to a normal rate. In spite of this, the patient made an uninterrupted recovery.

The volume of transfusion required.—Blood loss slightly over a litre is well tolerated (Wallace and Sharpey-Schafer). We have seen and measured directly blood loss of over two litres and, if our methods are correct, circulating blood volumes under two litres are not uncommon in severe shock. We therefore consider that transfusions of two litres or more are usually essential if the blood-pressure is 60 mm.Hg or below.

Morphine may conceivably be harmful in cases of severe oligæmic shock. It has been our experience that patients who are severely collapsed do not complain of pain, but as the blood-pressure recovers the patient tends to become more restless and pain perception is increased. We therefore do not give morphine in the stage of profound collapse, but as the patient recovers and pain is complained of, morphine is given in ordinary therapeutic doses.

REFERENCES

BLALOCK, A., and MASON, M. F. (1941), *Arch. Surg.*, **42**, 1054.
GRANT, R. T., and REEVE, E. B. (1941), *Brit. M. J.* (ii), 293.
WALLACE, J., and SHARPEY-SCHAFER, E. P. (1941), *Lancet* (ii), 393.

Dr. M. D. Nosworthy: It is now agreed that it is seldom wise to operate upon a patient while he is in shock; there being no doubt that effective resuscitation will convert such a patient from being a bad operative risk into a fair one. In fact, first-class resuscitation has given excellent results in spite of second-class surgery and third-class anæsthesia. There is some evidence, however, that, when a limb is so mangled that it will have to be amputated sometime, unless resuscitation produces an immediate and dramatic improve-

ment in the patient's condition the operation is better performed at once while the intravenous therapy is continued.

When immediate anæsthesia is called for, the lightest possible plane of narcosis—compatible with the nature of the operation—must be employed. This degree of anæsthesia will be obtained with a very much smaller concentration of *any* anæsthetic agent than would be required for the same individual in normal health. The concentration must also be built up very slowly in order to avoid overdosage which would be likely to result in the immediate or ultimate death of the patient.

Clinical experience is, at present, the best guide as to what resuscitative measures should be taken, and is essential for the correct interpretation of scientific data. This clinical judgment will be more quickly gained by personally following patients all through their illness, than by treating a far greater number merely during the pre-operative phase. The anæsthetist is in the best position to determine what supportive measures should be adopted during the operation itself. His responsibility, however, should not begin and end in the theatre; his opinion is of value in the resuscitative and post-operative phases as well. I am, therefore, doubly in favour of the resuscitation and recovery wards being adjacent to the theatre. Continuity of treatment by the same individual is, I believe, very important in the interests of the shocked patient.

It is obvious that in the case of a young soldier who was hungry, dehydrated, cold, wet, tired and very possibly frightened before he was wounded, there will be more response to simple treatments like hot drinks, warmth, rest and reassurance than there would be in the case of an older civilian whose injury alone—without any predisposing or contributory factors—has produced an identical degree of shock. I am going to confine my remarks on resuscitation to points which I think should be stressed by anæsthetists.

Morphine is often prescribed empirically. Pain, of course, must be relieved; patients with the most extensive injuries, however, are often in no pain, and yet they are well-meaningly given large and repeated injections of morphine. I do not believe that morphine has any specific anti-shock value. So long as the patient is in no pain and is at rest the advisability of giving sedatives is, in fact, doubtful. The use of morphine in such a case is likely to increase any anoxia present since the undesirable results of respiratory depression more than offset any decrease in metabolic rate. Frail patients have been admitted to hospital having had as much as one grain of morphine, and have really died of morphine overdosage. The dose should be individualized. Half a grain is the standard dose at some first-aid posts, and this is too much for many patients. An adequate sedative effect can be obtained, without the same respiratory depression, by giving an injection of scopolamine with a much smaller dose of morphine. Scopolamine, in contrast to morphine, helps to allay fear, and it is common knowledge —to anæsthetists anyway—that anxiety makes a patient much more susceptible to shock-producing factors. Reassurance of the patient is an important point which is usually neglected. Since the actual time of operation is often doubtful it is better to omit premedication; the anæsthetist can then give an intravenous injection of whatever morphine and scopolamine he may think fit in the theatre.

Restlessness is a common sign of oxygen want. Since other methods of resuscitation are always used concurrently the exact value of oxygen therapy in shock is difficult to assess. I have personally, however, so often seen during operations incipient circulatory depression relieved by an increase in the alveolar oxygen tension, that I believe that efficient oxygen therapy may be invaluable in breaking the vicious circle which develops in shock. It is, after all, anoxia that finally kills the shocked patient. Oxygen therapy offsets to some extent the disadvantages of heavy morphine sedation. When restlessness, unassociated with pain, persists in spite of resuscitation, it is better controlled, in my opinion, by intravenous paraldehyde than by morphine. Enough has been written already on how to administer oxygen. All I will say is that the earlier efficient oxygen therapy is started the greater and quicker will be the benefit therefrom. After starting with a high concentration in order to ascertain how great an improvement in the patient's condition can be obtained with oxygen, the alveolar tension should then be lowered little by little—provided the maximum benefit is still maintained—until atmospheric conditions have finally been restored. This procedure should also be followed during anæsthesia. When a high tension of oxygen has had to be used all through an operation, oxygen therapy should be fixed up in the theatre and continued in the recovery ward, until such time as a reduction in oxygen tension is no longer followed by an increase in pulse-rate. Economy in oxygen consumption is obviously desirable in these days, but it is not only for this reason that the minimum increase in oxygen tension which produces the maximum benefit is advised.

The importance of moving a shocked patient as little and as gently as possible cannot be over-emphasized. The foot of the bed should be raised a good eighteen inches

from the ground. This applies also to patients with chest injuries; if such a patient is more comfortable and less dyspnœic when propped up, then his head and shoulders can be raised while the foot of the bed is still blocked. During operation the table should be tilted into a slight Trendelenburg position. Hot drinks may be given with advantage right up to the time of operation except when laparotomy is to be performed.

The blood-pressure level is often a most unreliable guide to the patient's true condition. Patients can pass into the shocked state in a variety of ways. Not all, by any means, show the progressive fall in blood-pressure with increasing pulse-rate which is classically described. For example, the circulation in some way may quickly collapse, the pulse becoming impalpable and the blood-pressure unrecordable. This condition is often seen when a patient loses a considerable amount of blood rapidly—as for instance, when the surgeon during a nephrectomy drops the renal pedicle. As a rule, the blood-pressure soon climbs up again, even without treatment. When, however, the loss has been excessive or recovery has been too slow, the vicious circle of shock gradually becomes established. If injured patients are admitted to hospital in the collapsed state their condition is such that they are likely to be treated at once, and energetically, by the most inexperienced. Although, as I have said, many would pick up on their own, the group as a whole are probably more fortunate than some others who may not be treated seriously until the shock cycle is already well under way. Other patients, who have lost perhaps two pints of blood more slowly, may show no fall in blood-pressure and no increase in pulse-rate. But if patients, who—by their own defence mechanism only—have maintained or regained their blood-pressure in spite of considerable hæmorrhage, sustain further blood loss, they are likely to pass straight into "shock"—the fall in blood-pressure sometimes being almost a terminal event.

After a patient has been resuscitated by intravenous therapy prior to operation, it is a wise precaution to keep the drip running if the nature of the proposed surgery is likely to be severe, because it may be impossible to resuscitate the patient a second time if shock is permitted to return.

Blood and plasma transfusions are so easily obtainable nowadays that they are frequently given when they are not essential. When I judge, however, that the particular patient's powers of compensation are being, or are likely to be, overtaxed by blood loss or trauma, I always give intravenous therapy irrespective of the blood-pressure readings. The vicious circle may then be stopped before it has gathered momentum. I have observed on several occasions during operation deterioration and subsequent improvement in the feel of the pulse without change in either the systolic or diastolic pressures, or change in the pulse-rate. I cannot explain this finding, but I think that it may be of some importance since this change in the feel of the pulse has coincided with my appreciation of a change in the patient's condition on other grounds.

When it has been decided to give intravenous therapy, it will be found that—even if blood is ultimately to be used—it is better to start with plasma which runs much more readily into the veins of a shocked patient. Rapid resuscitation has two great advantages—it may relieve tissue anoxia before irreversible capillary damage has taken place, and it may also permit the patient to be operated upon within the "safe" period. The rates of flow and the amounts of transfusion have already been discussed by Dr. Grant. It is obvious that a patient who has recently lost much blood may safely be given a larger transfusion at a quicker rate than one who has lost little. When the rate of improvement, however, becomes disproportionately slow to the quantity of fluid being introduced, I think it may be wiser to discontinue intravenous therapy even though the plateau reached by the blood-pressure is still on the low side.

With regard to the critical blood-pressure level about which Dr. McMichael spoke I think the pulse pressure is important. I should be much happier about a patient with a pressure of 80/50 than with one of 90/75 mm.

Much has been written by laboratory workers on the effects of different anæsthetic agents in shock. Their conclusions, however, are often misleading since they do not always possess the necessary clinical experience to avoid confusing drug effects with shock. Furthermore, the condition of low blood-pressure which they produce in their experiments does not necessarily reproduce all the changes which occur in shock. It would appear reasonable to suppose that anæsthetic techniques which increase the area of the vascular bed would be harmful, and likewise those during the administration of which the alveolar oxygen tension is low. The deleterious effects of one agent at a certain depth, however, may not be operative at a lighter plane of anæsthesia, so that this agent, although bad for one type of operation, may be satisfactory for another. Again, there are probably several initiating factors in shock, and a different factor may be the chief one in different cases. Anæsthetic agents may produce different results depending upon which factor is uppermost in the particular case, and also upon the degree of shock present.

There seems to be no general agreement on the definition of shock. What one observer calls shock, another will not. Until we are all talking about the same entity, or distinguishing between different conditions, which ultimately present much the same clinical picture, we are attempting treatment before making an accurate diagnosis. If I were asked what anæsthetic technique I would use for thyroid surgery, I should first find out what was the matter with the patient. Thyroid operations are performed for various conditions, and each condition—apart from its individual variations—presents a different anæsthetic problem, and, in my opinion, each calls for a different method of approach. I believe much the same applies to shock. I want to know what has set the vicious circle of capillary atony in motion, and how far the process has progressed; whether the shock cycle is now, so to speak, self-generating, or whether initiating factors are still operating. In my view, we must first—making use of every means at our disposal—analyse cases and try to decide what factors are at work, and which is the predominant one in a given case—whether it be straight blood or fluid loss, the effects of trauma or afferent stimulation, exposure or anxiety, asphyxia or other factor. We also badly need criteria by which different degrees of shock development can be uniformly recognized. Then, in time, we may be in a position to say which is the best anæsthetic technique—and incidentally, the best method of resuscitation too—for a particular type of case.

Here is the anæsthesia record of one patient which may help to emphasize a few points.

A nervous man of 38 underwent a partial gastrectomy one morning in 1938. During the operation, which took just under two hours to complete, nothing of note occurred. The patient sustained little blood loss, was subjected to the minimum of trauma, and required no supportive treatment. At 11 o'clock, after the anæsthetic had been stopped, his blood-pressure was 150/100 and his pulse-rate 72. During the course of the afternoon he vomited bright blood on three occasions, the total quantity of blood lost being estimated at between 2½ and 3 pints. Treatment consisted of rectal salines and three injections of morphine gr. ¼. At 5.30 he was taken back to the theatre for exploration, and I was called to anæsthetize him. At that time he had a pulse-rate of 140 and a blood-pressure of 70/50. The patient was transferred from his bed to the operating table, and this handling made his blood-pressure become unrecordable and increased his pulse-rate to 170. I gave him 100% oxygen to breathe, and by the time the blood transfusion had been set up—and before any benefit could have been derived from it—his pulse-rate had dropped to 130 and his blood-pressure had risen to 90/70. Of course, he had had time to rally from the effects of being moved, but since his pulse-rate was now lower and his blood-pressure higher than they had been in bed I think the oxygen was in no small measure responsible for his improvement.

At this point, making use of the carbon dioxide absorption technique—which several of my correspondents have also found beneficial for shocked patients—I anæsthetized him with cyclopropane and oxygen. The anastomosis was unpicked and resutured in thirty-five minutes and, as you can see, the improvement in his condition was maintained. To guard against possible restlessness I kept him anæsthetized for a further twenty-seven minutes, until he had received two pints of blood. During the last half-hour I was able steadily to lower his alveolar oxygen tension, until, when the anæsthetic was discontinued, he was breathing air, was awake, and had a pulse-rate of 104 and a blood-pressure of 106/70. His convalescence was then straightforward.

During the six and a half hour interval between this man's two appearances in the theatre I have no data about his condition. It happens too often that promising material like this is wasted from the research point of view owing to lack of accurate detailed observations.

Although this man displayed all the classical signs of shock, his rapid recovery was not like that of a truly shocked patient. Even if the same vicious circle eventually becomes established in both, I wonder whether a case of external hæmorrhage pursues the same course as a case of shock from other causes. There is no doubt that the effects of blood loss, if treated in time, can be largely removed by oxygen therapy and blood transfusion. Therefore, cases in which external hæmorrhage is the chief factor are comparatively easy to treat. In other cases, resuscitation has to overcome factors which are still militating against it. Some factors can be overcome in time, others cannot. Others, again, can only be eradicated by surgery. The benefit likely to be derived from operation, however, must be weighed against the risk of exposing the patient to further hæmorrhage, fresh trauma, and—unless anæsthesia is skilfully administered—also to the shock and asphyxia associated with a bad anæsthetic.

VOL. XXXV. NO. 1. NOVEMBER, 1941.

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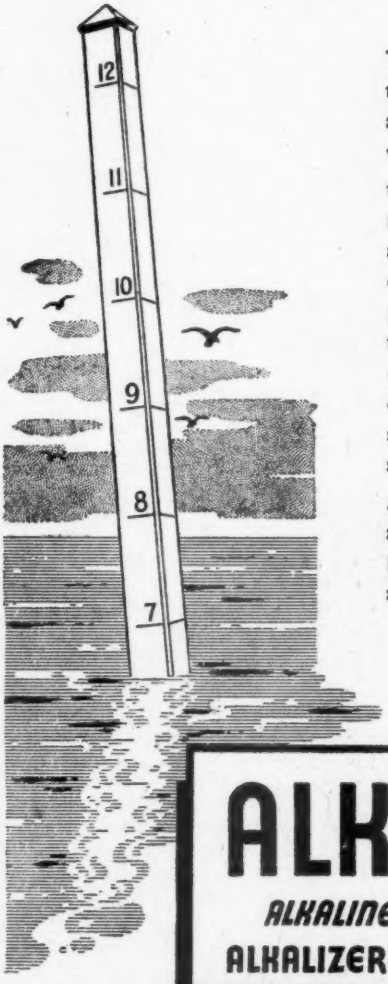

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